Anaesthesia

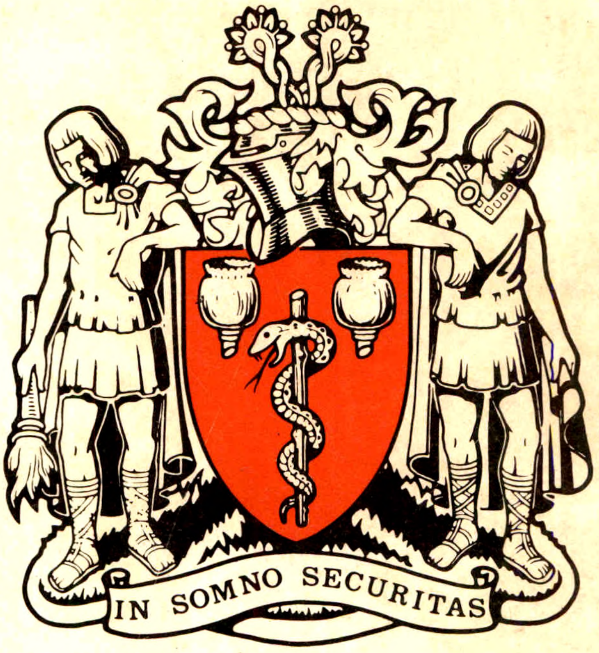
Journal of the Association of Anaesthetists of Great Britain and Ireland

Volume 44 Number 8 August 1989

VOL-44
NO. 08-9
1989

CUK-H02479-11-P024527

11

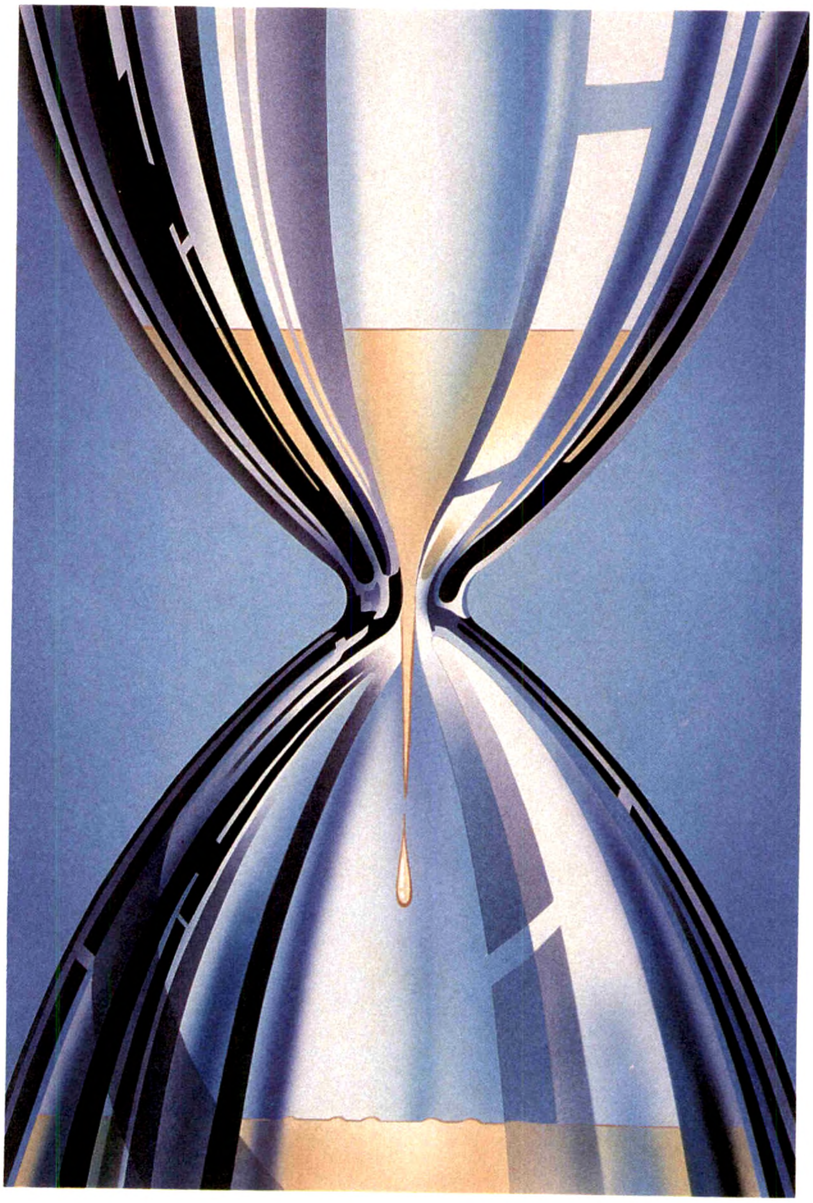


The Association of Anaesthetists of Great Britain and Ireland
Patron: HRH The Princess Margaret, Countess of Snowdon

Published for the Association by
Academic Press Grune & Stratton
London San Diego New York Boston
Sydney Tokyo Toronto

ISSN 0003-2409

Predictable in IV sedation.



P, 24,527

DUMEX

Diazemuls®

10mg diazepam in 2ml emulsion

The cream of IV sedation

PRESCRIBING INFORMATION

PRESENTATION Ampoules of a white opaque emulsion containing diazepam BP 10mg in 2ml.

Indications:

1. Sedation prior to procedures such as endoscopy, dentistry, cardiac catheterisation and cardioversion.
2. Premedication prior to general anaesthesia.
3. Control of acute muscle spasm due to tetanus or poisoning.
4. Control of convulsions; status epilepticus.
5. Management of severe acute anxiety or agitation including delirium tremens.

DOSAGE AND ADMINISTRATION

Diazemuls may be administered by slow intravenous injection (1ml per min), or by continuous infusion. Diazemuls should be drawn up into the syringe immediately prior to administration.

1. **Sedation:** 0.1 – 0.2 mg diazepam/kg body weight by iv injection.
2. **Premedication:** 0.1 – 0.2 mg diazepam/kg body weight by iv injection.
3. **Tetanus:** 0.1 – 0.3 mg diazepam/kg body weight by iv injection repeated every 1 – 4 hours as required. Alternatively, continuous infusion of 3 – 10 mg/kg body weight every 24 hours may be used.
4. **Status epilepticus:** An initial dose of 0.15 – 0.25 mg/kg body weight by iv injection repeated in 30 to 60 minutes if required, and followed if necessary by infusion of up to 3 mg/kg body weight over 24 hr.
5. **Anxiety and tension, acute muscle spasm, acute states of excitation, delirium tremens:** The usual dose is 10 mg repeated at intervals of 4 hours, or as required.

Elderly or debilitated patients: Elderly and debilitated patients are particularly sensitive to benzodiazepines. Dosage should initially be reduced to one half of the normal recommendations.

CONTRA-INDICATIONS, WARNINGS, ETC:

As with other benzodiazepine preparations: should not be used in phobic or obsessional states nor in the treatment of chronic psychosis. Treatment with diazepam may cause drowsiness and increase the patient's reaction time. Use with caution in patients with impairment of renal or hepatic function and in patients with pulmonary insufficiency or myasthenia gravis. Should not be used alone to treat depression or anxiety associated with depression. Amnesia may occur. In cases of loss or bereavement psychological adjustment may be inhibited by benzodiazepines. Disinhibiting effects may be manifested in various ways. Suicide may be precipitated in patients who are depressed and aggressive behaviour toward self and others may be precipitated. Extreme caution should therefore be used in prescribing benzodiazepines in patients with personality disorders. Physiological and psychological symptoms of withdrawal including depression may be associated with discontinuation of benzodiazepines even after normal therapeutic doses for short periods of time.

Pregnancy and Lactation: Diazepam crosses the placenta an should not be used during pregnancy unless considered essential. Large maternal doses administered during delivery may produc clinical effects in the newborn. Diazepam can be transmitted in brea milk and clinical effects may occur in the breast-fed infant.

Side Effects: May rarely cause local pain or thrombophlebitis. Ra instances of a local painless erythematous rash around the site injection. Urticaria and, rarely, anaphylaxis have been reported.

Overdosage: CNS depression and coma. Treatment symptomatic.

PHARMACEUTICAL PRECAUTIONS: See Data Sheet

Pack Size & Cost: 10 × 2ml ampoules: NHS Price £6.29

Product Licence No: 10183/0001

Date of preparation: April 1989

(Diazemuls is a registered trademark)

Product Licence Holder: Dumex Ltd.,
Riverside Way,
UXBRIDGE,
Middx. UB8 2YF
Tel: Uxbridge (0895) 51144

Distributed in the UK by KabiVitrum Ltd

John Alfred Lee

Anaesthesia, 1989, Volume 44, page 631

Editorial

John Alfred Lee (1906–1989) MRCS, LRCP, MMSA, FFARCS, FFARCSI (Hon)

Past President of the Association of Anaesthetists of Great Britain and Ireland

Alfred Lee was born in Liverpool in 1906, the eldest son of a well-known Noncomformist minister. He was educated at Taunton School in Somerset and then as a medical student at the University of Durham College of Medicine in Newcastle on Tyne. Here, he qualified as a doctor in 1927 at the age of 21. He spent the next 2 years in resident appointments, first as Resident Medical Officer at the Princess Mary Maternity Hospital and then at the Royal Victoria Infirmary in Newcastle. He decided to become a family doctor and bought a share of a partnership in Southend-on-Sea by paying for it out of income. His interest in practical anaesthesia started while he was a house surgeon and he was soon appointed as a general practitioner anaesthetist at the Southend Victoria Hospital, being one of the first two anaesthetists ever appointed in the town; this was in 1931. The next year he occupied a similar post at the new Southend General Hospital. During the second world war he became a whole-time anaesthetist in the Emergency Medical Service and served for 5 years in this capacity at the Runwell Emergency Hospital in Essex. In 1947 he became consultant anaesthetist to the Southend General Hospital and remained in this post until his retirement.

He originated at Southend the first Anaesthetic Outpatient Department in any British hospital in 1948, and in 1955 organised the first Postoperative Observation ward (Recovery ward) in any British general hospital. This latter innovation gave him cause for the greatest of all his satisfactions, almost greater than that from his literary achievements, because it was the first in the United Kingdom. He served as Clinical Tutor at Southend from 1972 until 1976.

He took his share in the corporative activities of the specialty and served as President of the Section of Anaesthetics of the Royal Society of Medicine in 1959 and received its Henry Hill Hickman Medal in 1976. He was elected as President of the Association of Anaesthetists of Great Britain and Ireland (1972–73) and also as an honorary member of the Association. He was on two occasions elected onto the Board of the Faculty of Anaesthetists, served as an examiner for the final FFARCS examination, was Joseph Clover Lecturer in 1960 and Faculty Medallist in 1976. In 1970 he became an honorary Fellow of the Faculty of Anaesthetists of the Royal College of Surgeons in Ireland.

Alfred Lee, since retiring in 1971 from his post in the NHS, continued to write, to teach in Britain, in Holland and in Baghdad, to lecture and to give anaesthetics.

In 1947 he was responsible for the first edition of a small book *A synopsis of anaesthesia*. The book has been translated into seven foreign languages and has remained in print for 40 years, the 10th edition (written with two colleagues) was published in 1987. He was also part author of *Lumbar puncture and spinal analgesia* editions three, four and five (1985), the first two editions of which were the work of Professor Sir Robert Macintosh. He was, in addition, responsible for other books and articles dealing with the specialty. He acted as an Assistant Editor of the journal *Anaesthesia* and between 1970 and 1972 he was Chairman of its Editorial Board.

In 1984 he received the first Carl Koller Gold Medal of the European Society of Regional Anaesthesia on the centenary of the first use of local analgesia in Vienna; in 1985 he gave the Gaston Labat Lecture before the American Society of Regional Anaesthesia in Washington, D.C., the Stanley Rowbotham Lecture at the Royal Free Hospital in London and the T. H. Seldon Distinguished Lecture before the International Anesthesia Research Society in Las Vegas in 1986. In 1986, he and a hospital administrator published a substantial volume dealing with the history of the hospitals of Southend.

His marriage to Norah (née Sandison) took place in 1930 and they have a son who is a doctor, and a daughter.

J. A. Lee

The above clear and factual account was written three years ago by Alfred Lee. The precise nature of it reflects his personality so well that the Editor decided to publish it unadorned by another's prose. It does, however, remain to be said that Alfred Lee was one of the most loyal and devoted supporters our discipline has ever known. Right up to the year of his death he was to be seen at public meetings, listening and learning and passing on his experience to younger doctors.

He was, however, not merely active professionally but also culturally. He had a passionate love of opera, shown by repeated visits with his wife to Bayreuth and Munich, to say nothing of his regular attendance at Glyndebourne. His memory was legendary and he was still able to answer most of the questions on BBC Mastermind; but he was gloomy about the current prospects of Newcastle United football team which he had supported all his life!

His son describes him as 'essentially shy and introverted; he overcame a terror of public speaking and became very good at it'.

It is particularly fitting also to record the encouragement and support he gave to the current and the previous Editors of this journal. He missed little and, if he had comment to make, we were certain to receive a neatly typed communication postmarked Southend within days of the appearance of the journal. We salute his memory and pass our sympathies to his widow and family.

J. N. Lunn

0003–2409/89/080631+01 $03.00/0 © 1989 The Association of Anaesthetists of Gt Britain and Ireland

Anaesthesia, 1989, Volume 44, pages 632–634

Fluid deprivation before operation

The effect of a small drink

A. AGARWAL, P. CHARI AND H. SINGH

Summary

The effect of oral fluids before operation, followed by intramuscular morphine, on gastric volume and pH was examined in 150 elective surgical patients, ASA physical status 1 and 2, who were randomly assigned to one of the three groups of 50 each. Group 1 (control) continued their overnight fast; patients in Groups 2 and 3 received 150 ml water 2 hours before the scheduled time of surgery. Patients in Group 3 received intramuscular morphine 0.15 mg/kg and promethazine 0.5 mg/kg one hour before operation. The residual gastric volume was obtained by suction and its volume and pH measured immediately after induction of anaesthesia. Statistically significant ($p < 0.05$) decrease in residual gastric volume was observed in Groups 2 and 3 as compared to Group 1. However, the difference between these two groups was not statistically significant. There was no statistically significant difference in pH among the three groups. Overnight fluid fasting is not justified in elective surgical patients. Morphine can be safely given one hour before surgery in patients who have received water (150 ml) 2 hours before operation.

Key words

Gastrointestinal tract; stomach, pH, volume.
Fluid balance; oral fluids.

Patients, during the first 80 years of anaesthesia, were encouraged to take oral fluids until 3 hours before elective surgery.[1–4] The fluid was specified as glucose water, beef tea or china tea. Solid food was withheld for a longer period. These guidelines are consistent with our knowledge of gastric physiology. Water and isotonic fluids, which do not require digestion, pass through the stomach very rapidly; half of a 750-ml bolus disappears in approximately 20 minutes.[5] The rate of gastric emptying for solid food on the other hand varies considerably: the gastric emptying half-time ranges up to nearly 5 hours and the complete emptying time is up to 12 hours.[6,7] Prolonged fasting before operation does not ensure an empty stomach. One third of patients who fasted for 7–22 hours still have residual gastric volume (RGV) of 25 ml or more, with a pH 2.5 or less.[8]

The current recommendation for fasting before operation does not take this difference of emptying time into account. A 4 to 6 hours fast for liquids as well as solids,[9,10] or simply nothing by mouth after midnight[11] is now established practice. There appears to be no scientific basis for this extended period of fluid deprivation in elective patients. Recently various studies observed the effectiveness of 150 ml water given orally 2–3 hours before operation over a prolonged overnight fast in lowering RGV and raising pH in a greater percentage of patients.[12–15]

We addressed two issues in this study. First, is an overnight fluid fast justified in elective surgical patients? Second, can narcotic premedication be given to patients who have received 150 ml water 2 hours beforehand?

Methods

The study protocol was approved by an ethics committee. Informed consent was obtained from 150 patients scheduled for elective surgical procedures aged between 15 and 60 years, and ASA of physical status 1 and 2. Pregnant, emergency and outpatients were excluded from the study; patients who were receiving drugs known to affect gastric secretion or motility were also excluded.

Consecutive patients were stratified by sex and randomised to one of the three groups using a table of random sampling numbers.[16] Patients graded the severity of their hunger and thirst as nil, slight, moderate or severe immediately before randomisation.

The control group continued their overnight fast: nothing by mouth after 2200 hours (Group 1). Patients in Groups 2 and 3 received 150 ml plain water 2 hours before the scheduled time of surgery. Patients in Group 3 also received intramuscular morphine 0.15 mg/kg and promethazine 0.5 mg/kg one hour before operation. Fluids before operation and premedication were prescribed by the person designated to anaesthetise the patient and not by the investigator who was unaware of the allocation to groups.

A. Agarwal, MD, Lecturer, P. Chari, MD, MAMS, Associate Professor, H. Singh, MS, DA, FAMS, Professor, Department of Anaesthesia, Postgraduate Institute of Medical Education and Research, Chandigarh 160012, India.

Accepted 15 February 1989.

0003–2409/89/080632+03 $03.00/0

© 1989 The Association of Anaesthetists of Gt Britain and Ireland

Table 1. Patient characteristics mean (SD).

	Age (years)	Weight (kg)	Overnight fast (hours)	Ingestion–induction interval (minutes)
Group 1	36.2 (10.4)	58.1 (9.2)	11.8 (2.5)	—
Group 2	34.3 (12.4)	56.5 (8.5)	12.2 (2.1)	151 (21)
Group 3	35.6 (12.8)	57.7 (8.9)	12.1 (2.9)	153 (22)

Patients again graded their hunger and thirst on arrival in the operating room. Nausea and vomiting after the premedication were noted. General anaesthesia was induced in all patients who had intravenous thiopentone followed by suxamethonium and tracheal intubation. Nitrous oxide and oxygen supplemented by halothane were used for maintenance. An 18-FG Salem-sump tube was passed into the stomach just after induction and intubation, and its position confirmed by auscultation of injected air. Gastric fluid was obtained with the patient in a supine position and with the sampling tube in several locations within the stomach, by aspiration into a 60-ml syringe. The investigator who aspirated the stomach was unaware as to which group the patient had been assigned. The volume of the fluid was recorded and its pH measured by calibrated Corning 150 pH meter.

The data were analysed using Student's unpaired *t*-test. Correlation of patient characteristics with RGV and pH was sought using linear regression analysis. Differences were considered statistically significant when $p<0.05$.

Results

All three groups were comparable with respect to age, weight, fasting interval and ingestion–induction interval (Table 1). There was no difference in the incidence of smoking, heartburn and dyspepsia among the groups.

The volume and pH of gastric contents are shown in Table 2. Patients who received 150 ml water with or without morphine (Groups 2 and 3) had a significantly lower RGV compared with those who remained fasting ($p<0.05$). However, the difference between these two groups was not statistically significant. Slight increase in pH was observed in Groups 2 and 3 (Table 2), but this increase was neither clinically nor statistically significant.

More patients had an RGV greater than 25 ml in the fasting group (Group 1) than in those who had received 150 ml water with (or without) intramuscular morphine, $p<0.05$ (Table 3). There was, however, no statistically significant difference between the numbers of patients who had a gastric $pH<2.5$ in any group (Table 3). The incidence of patients with the combined high risk factors of RGV greater than 25 ml and pH less than 2.5 was significantly ($p < 0.05$) decreased by the intake of 150 ml water (Group 2). Administration of morphine after ingestion of 150 ml water (Group 3) also resulted in a statistically significant decrease in the incidence of combined high risk factors. There was no difference in the incidence of combined high risk factors between Groups 2 and 3.

Table 2. Gastric fluid volume and pH.

	Volume (ml)		pH	
	Mean (SD)	Range	Mean (SD)	Range
Group 1	29.9 (18.2)*	0–75	1.85 (1.26)	1.17–5.4
Group 2	20.6 (14.1)	0–50	2.05 (1.41)	1.21–5.82
Group 3	22.3 (10.5)	0–62	2.06 (1.34)	1.22–5.80

*$p < 0.05$ group 1 as compared with groups 2 and 3.

Table 3. Incidence of patients with risk factor for acid-aspiration syndrome.

	Volume >25 ml		pH <2.5		Volume >25 ml and pH <2.5	
	n	%	*n*	%	*n*	%
Group 1	31/50*	62	45/48	93.75	28/50*	56
Group 2	18/50	36	41/46	89.13	16/50	32
Group 3	18/50	36	40/45	88.88	16/50	32

Denominators in the pH column are the patients from whom gastric aspirate was obtained.
*$p<0.05$ group 1 as compared with groups 2 and 3.

The changes in the severity of hunger and thirst are shown in Table 4. Significantly more patients who had a drink (Groups 2 and 3) became less hungry ($p < 0.05$) and less thirsty ($p < 0.05$), but patients who continued to fast became more thirsty compared with those who received 150 ml water with or without morphine (Groups 2 and 3).

There was no correlation of RGV or pH with age, weight, sex, duration of fast and ingestion–induction interval. No patient had nausea or vomiting.

Discussion

Pulmonary aspiration of gastric contents during anaesthesia is a small but significant cause of anaesthesia-related deaths.[17,18] Precise numbers are not known, but it is probable that many patients suffer nonfatal aspiration with significant morbidity. The severity of pulmonary damage is related both to the volume and pH of the inhaled fluid. A combination of gastric volume more than 25 ml, with a pH of less than 2.5 is considered potentially lethal[19] should aspiration occur. Any safe treatment or management that reduces this hazard is desirable.

Recently several workers observed that 150 ml water given 2 to 3 hours before surgery was effective in lowering RGV and raising pH in a greater percentage of patients.[12–15] None of these patients received narcotic premedication because opiates are potent antagonists of gastric emptying. As far as we are aware, the present study is the first to investigate the effect of narcotic premedication on RGV and pH in patients who received 150 ml water 2 hours before surgery.

Table 4. Changes in hunger and thirst: effect of oral fluid.

	Hunger			Thirst		
	Less	More	No change	Less	More	No change
Group 1	4*	9	37	1*	16*	33
Group 2	11	8	31	27	3	20
Group 3	10	8	32	28	2	20

Hunger and thirst on arrival in operating room compared with 2 hours beforehand.
*$p<0.05$ group 1 as compared with groups 2 and 3.

The RGV recorded in this study was the volume aspirated through an 18-FG Salem-sump tube. The volume of gastric juice aspirated using this tube is a very good estimate of total volume of gastric residue.[20] The error from the method of sampling, if any, should be small and consistent in all groups. This method allows for valid comparison of our results with those of other investigators who used similar methods.

The observed increase in pH could be a result of dilution of fasting gastric acids with ingested water. The observed decrease in RGV after intake of water in Group 2, may be due to stimulation of gastric motility caused by the entry of the cold fluid, or by the physical distension of the stomach, or both. The similar decrease in RGV observed in Group 3, could be due to the fact that by the time the intramuscular morphine starts to reduce gastric emptying, the ingested fluid would have already passed out from the stomach, as observed by earlier workers; half of a 750-ml bolus of water leaves the stomach in approximately 20 minutes.[5]

There was no change in the severity of their hunger or thirst in the 2 hours before surgery in approximately half of all the patients. However, in patients who were given oral fluids and the group in whom the drink was followed later with intramuscular morphine and promethazine, the degree of hunger and thirst decreased significantly in more patients than in the fasting group. None of the patients had nausea or vomiting.

Thus our findings suggest that, in elective surgical patients, prolonged fluid fasting is not justified. Water (150 ml) given orally 2 hours before operation produces a lower RGV and higher pH than does a prolonged overnight fast. Water (150 ml) given 2 hours before surgery can even be followed safely by intramuscular morphine and promethazine one hour before the scheduled time of surgery with a similar decrease in RGV and increase in pH.

References

1. Snow J. *On chloroform and other anaesthetics.* London: Churchill, 1858: 74–5.
2. Lister J. On Anaesthetics, Part III. In: *Holmes' system of surgery, Vol. III,* 3rd edn. London 1883. (Reprinted in: *The collected papers of Joseph Lister.* Birmingham: The classics of medicine library, 1979; 171–2.)
3. Buxton DW. *Anaesthetics: their uses and administration.* London: Lewis, 1920: 24–5.
4. Boyle HEG, Hewer CL. *Practical anaesthetics,* 3rd edn. London: Frowde, Hodder and Stoughton, 1923: 9.
5. Moore JG, Christian PE, Coleman RE. Gastric emptying of varying meal weight and composition in man. Evaluation by dual liquid-and solid phase method. *Digestive Diseases and Sciences* 1981; **26:** 16–22.
6. Hunt JN. Some properties of an alimentary osmoreceptor mechanism. *Journal of Physiology* 1956; **132:** 267–88.
7. Horowitz M, Pounder DJ. Is the stomach a useful forensic clock? *Australian and New Zealand Journal of Medicine* 1985; **15:** 273–6.
8. Sutherland T, Davies JM, Stock J. The price and value of preoperative outpatient fasting—effects on gastric contents and outpatient morbidity. *Canadian Anaesthetists' Society Journal* 1985; **32:** S100.
9. Atkinson RS, Rushman GB, Lee JA. *A synopsis of anaesthesia,* 9th edn. Bristol: Wright 1982: 96.
10. Gregory IC. Anaesthesia and gastro-intestinal tract. In: Churchill-Davidson HC, ed. *A practice of anaesthesia,* 9th edn. Chicago Year Book Medical Publishers, 1984: 939–53.
11. Orkin FK. Selection. In: Wetchler BV, ed. *Anaesthesia for ambulatory surgery.* Philadelphia: Lippincott, 1985: 106.
12. Sutherland AD, Maltby JR, Sale JP, Reid CRG. The effect of preoperative oral fluid and ranitidine on gastric fluid volume and pH. *Canadian Journal of Anaesthesia* 1987; **34:** 117–21.
13. Prior FM. *A manual of anaesthesia for small hospital.* New Delhi: Emmanuel Hospital Association 1974: 58–9.
14. Hjortso E, Mondorf T. Does oral premedication increase the risk of gastric aspiration? A study to compare the effect of diazepam given orally and intramuscularly on volume and acidity of gastric aspirate. *Acta Anaesthesiologica Scandinavica* 1982; **26:** 505–6.
15. Maltby JR, Sutherland AD, Sale JP, Shaffer EA. Preoperative oral fluids: is a five-hour fast justified prior to elective surgery? *Anesthesia and Analgesia* 1986; **65:** 1112–6.
16. Hill AB. *A short text book of medical statistics,* 10th edn. London: Hodder and Stoughton, 1977: 302–12.
17. Department of Health and Social Security. *Report on confidential enquiries with maternal deaths in England and Wales 1976–78.* London: Her Majesty's Stationery Office 1982: 96–100.
18. Lunn JN, Mushin WW. *Mortality associated with anaesthesia.* London: Nuffield Provincial Hospitals Trust, 1982.
19. Robert RB, Shirley MA. Reducing the risk of acid aspiration during cesarean section. *Anesthesia and Analgesia* 1974; **53:** 859–68.
20. Maltby JR, Koehli N, Ewen A, Schaffer EA. Assessment of preoperative gastric emptying using a marker dye. *Canadian Journal of Anaesthesia* 1988; **35:** S63–4.

Anaesthesia, 1989, Volume 44, pages 635–640

The effects of hypocapnic ventilation on mental function in elderly patients undergoing cataract surgery

R. M. JHAVERI

Summary

Mental function was studied using the Rivermead Behavioural Memory Test and the Unprepared Simple Reaction Time test in 83 elderly patients for cataract surgery. Three groups of patients were studied: Group N (n = 40) whose lungs were ventilated to a mean $Pa\text{CO}_2$ *of 4.9 kPa, Group H (n = 30) who were hyperventilated to a mean* $Pa\text{CO}_2$ *of 2.9 kPa, and Group L (n = 13) who received local anaesthesia for surgery. The psychometric tests were administered on the day before the operation, and 4 days and 4 weeks after the operation. Statistically significant changes in the performance of hyperventilated patients could not be demonstrated using these tests.*

Key words

Memory.
Carbon dioxide; hypocarbia.

Controlled ventilation of the lungs during surgery is often associated with deliberate or inadvertent hypocapnia. Moderate hypocapnia ($Pa\text{CO}_2$ 4.0–4.7 kPa) is often employed in the belief that it contributes to the 'anaesthetic state',[1] and reduces the requirements of anaesthetic agents and muscle relaxant. However, hypocapnia produces cerebral vasoconstriction and a reduction in cerebral blood flow. Whether this produces impaired cerebral function is debated.

The reports of reduction in cerebral blood flow caused by hypocapnia[2] due to cerebral vasoconstriction[3,4] prompted Allen and Morris[5] to study the effect of hypocapnic hyperventilation using critical flicker fusion (CFF) frequencies. They found a reduction in CFF frequencies in their patients. The average duration of CFF depression was 1.5 days; one patient showed a reduced frequency for 3 days. They concluded that cerebral damage, although present, was slight in degree. Blundell[6] found that memory and mental organisation were impaired 'transiently' in elderly surgical patients. However, no attempt was made in this study to identify specific surgical or anaesthetic factors which may have caused this impairment. Wollman and Orkin[7] reported that the reaction time was prolonged in the hypocapnic group and that the difference was significant even on the sixth day. Hovorka[8] found deterioration in the psychometric performance of hyperventilated patients for 48 hours. Flatt *et al.*[9] detected impaired mental function after general anaesthesia with some patients failing to regain their pre-operative level of performance after 6 weeks. Standardisation of anaesthetic technique was not performed in this study; absence of hypocapnia was assumed, and whether hypotensive anaesthesia was used in these patients is not clear from the paper.

Whitwam *et al.*[10] on the other hand, did not find depression of CFF after hypocapnia. Blenkarn *et al.*[11] who used tests of cognitive function and Murrin and Nagarajan[12] who used the Wechsler Memory Scale also failed to detect impairment of performance in hyperventilated patients. Karhunen and Jönn[13] stated that 'general anaesthesia does not affect memory function more profoundly than local anaesthesia supplemented with tranquilising and/or analgesic drugs.'

Thus, the research so far conducted in this area has produced contradictory results. Many of these papers have suffered from a lack of standardisation of various surgical and anaesthetic factors that may affect postoperative mental function. Paid volunteers were used by some investigators in order to isolate anaesthetic factors from surgical influences. Such studies make a useful contribution, but their results are difficult to interpret because of a biased selection of subjects who are highly motivated to perform well.

The aim of the present study was to relate hypocapnia during operation to change in performance of cognitive function tests after operation.

R.M. Jhaveri, FFARCSI, Research Registrar, East Anglian Regional Health Authority, Cambridge.
Present appointment: Registrar, Department of Anaesthesia, The London Hospital, Whitechapel, London E1 1BB.
Accepted 16 February 1989.

0003–2409/89/080635+06 $03.00/0
© The Association of Anaesthetists of Gt Britain and Ireland

Methods

The protocol was approved by the District Ethics Committee.

Eighty-three patients, all over 60 years of age, admitted for cataract surgery were studied. They were visited and assessed by their consultant anaesthetists in the usual way on the day before the operation; the nature of the proposed study was explained to them, and informed consent obtained. No persuasion was applied for their inclusion in the trial or for continued participation, since the resultant anxiety might have affected their performance.

Diabetic patients were excluded because of the possibility that metabolic disturbance might cloud their performance in psychometric tests. Those patients who could not complete tests before operation because of severe visual impairment were also excluded.

Anaesthetic management

All patients were premedicated with oral temazepam 0.3 mg/kg, rounded off to 10 or 20 mg, 2 hours before surgery. Patients who were to receive general anaesthesia were randomly allocated by means of a random number table to either Group N or H. The lungs of patients in Group N were to be ventilated so as to achieve an arterial $P\text{CO}_2$ of 5.3 kPa, and Group H patients to achieve an arterial $P\text{CO}_2$ of 2.7 kPa.

General anaesthesia was induced with thiopentone 3–5 mg/kg. Muscle relaxation was achieved using atracurium 0.4 mg/kg, and fentanyl 1 μg/kg was given at induction. Anaesthesia was maintained with 66% nitrous oxide in oxygen supplemented with enflurane 0–1%.

A coaxial breathing system with a Penlon Nuffield 200 ventilator was used for artificial ventilation of lungs. The advantage of this arrangement is that the patients can be given constant and large tidal (and minute) volumes while the desired arterial carbon dioxide tension can be achieved by alterations in the fresh gas flow (FGF) alone, provided that the FGF is less than the total minute volume of ventilation.[14-16] Thus, at low rates of FGF, normocapnia will be achieved, even in patients of small body weight whose lungs are ventilated with large minute volumes. A flow rate of 0.5 litres/second and I:E ratio of 1.5:3.0 was maintained for all patients. A fresh gas flow of 70 ml/kg for patients in Group N, and 200 ml/kg for those in Group H was used. These flows were found to be appropriate so that the desired $P\text{aCO}_2$ of 5.3 and 2.7 kPa respectively were achieved in a pilot study of 20 patients.

Baseline ECG and indirect automatic blood pressure recordings were taken before induction of anaesthesia in the operating theatre. End-tidal carbon dioxide tension was monitored using a capnograph (Datex Normocap) once the patient was connected to the lung ventilator.

An alveolar–arterial carbon dioxide tension gradient of 0.7 kPa[17] was assumed and minor adjustments of the FGF were made 10 minutes into the operation, if necessary. An arterial blood sample was taken after insertion of the lens implant as a check that the required $P\text{aCO}_2$ was achieved.

Neuromuscular blockade was reversed with neostigmine and atropine. The patient received 28% oxygen by mask in the recovery room and for 2 hours afterwards.

Oral paracetamol provided sufficient postoperative analgesia for all but one patient who required a single intramuscular injection of papaveretum in the first hour after the surgery.

Those patients who were deemed to be unsuitable for general anaesthesia because of the presence of intercurrent cardiac and (or) respiratory disease, had local anaesthesia for the cataract extraction. These patients formed a third group (Group L) and were included in the study to allow for the effects of hospitalisation. They received 0.03 mg/kg midazolam after which the surgeon performed the retrobulbar block using 2% lignocaine. Further increments of 1 mg midazolam (diluted to a concentration of 1 mg/ml) were given if required, by the anaesthetist.

Psychometric tests

A variety of tests have been used to demonstrate deleterious effects of hypocapnia and anaesthesia. These include: psychiatric tests, such as interviews,[1] questionnaires[9,13] and personality tests,[1] psychological tests, such as Wechsler Adult Intelligence Scale,[6,9,13] Wechsler Memory Scale,[8,9,12,13] Raven Matrices,[6] Luria tests[13] and simple and disjunctive Reaction Time tests,[7-9,11] and physiological tests, such as Critical Flicker Fusion test[5,8,10] and electroencephalography.[18]

Mild degrees of cerebral hypoxia affect higher intellectual functions such as memory and learning ability.[7] Blundell[6] found deterioration in memory and organisation of thought in the postoperative period. The choice of psychometric tests is also governed by practical factors such as the availability of duplicate, standardised versions of the tests, the time necessary for administration of the tests, objectivity and ease of scoring.[19]

Thus, the following criteria were laid down for the selection of appropriate psychometric tests: they should measure memory, learning ability, speed of reaction and the ability to concentrate; they should be sensitive enough to measure small changes in mental function which are not clinically obvious; the learning effect due to repeated testing should be absent or minimal; they should be easy to learn for elderly patients; and the test battery should not take more than an hour to administer since the longer session may jeopardise patient cooperation.

The Rivermead Behavioural Memory Test (RBMT) and the Unprepared Simple Reaction Time (USRT) test were selected for the present study after discussions and expert psychological advice and guidance.

Rivermead Behavioural Memory Test[20]

This test battery detects impairment of the function of everyday memory. The subtests involve either remembering

Table 1. RBMT subtests.

1	First name
2	Second name
3	Belonging
4	Appointment
5	Picture recognition
6 a,b	Story recall — immediate and delayed
7	Face recognition
8 a,b	Remembering a route — immediately and after a delay
9 a,b	Deliver a message — immediate and delayed recall
10	Orientation
11	Date

to carry out some everyday task or retaining the type of information needed for everyday function. It consists of a number of subtests described in Appendix 1.

The subtests are listed in Table 1; of these, subtests 1–5, 6b, 7, 8b and 9b assess delayed recall; subtests 6a, 8a and 9a assess immediate recall; and subtests 10 and 11 assess orientation.

There are four parallel versions of these tests (of which the first three were used for the present study) so as to minimise the effect of practice with repeated testing.

Unprepared Simple Reaction Time

This is a test of the subject's speed of reaction as well as the ability to maintain concentration. The test is administered with a commercially available, portable reaction timer.[21]

The device displays a stimulus light in a window in response to which the subject presses a button as quickly as possible. The resulting reaction time (RT) is recorded on a magnetic tape cassette. The next stimulus is presented at unpredictable intervals which vary from 1 to 10 seconds. The cassette is subsequently 'read' by means of suitable computer software.

Two practice tests of 5 minutes each were given before a third, definitive test of 10-minutes duration. Approximately 70 RT values were thus obtained from each patient from each 10-minute test. These were scrutinised to eliminate nonsensical behaviour and a mean RT for that trial was calculated.

These tests were performed on the day before the operation (Test 1), and 4 days and 4 weeks after the operation (Tests 2 and 3). Of these, Test 3 was conducted when the patient attended for his (her) follow up outpatient appointment. The tests were administered by the author who was unaware of the $P\text{aCO}_2$ achieved during surgery. It proved impossible not to know the identity of the patients in the local anaesthetic group because of the tell-tale bruise caused by the necessary local anaesthetic injection. The performance in psychometric tests is thought to vary with environmental factors, such as temperature and time of day. Therefore, the tests were always carried out in the same room adjacent to the ward. Practical difficulties precluded performing the tests at the same time of day.

Table 2. Profile of patients in three groups. Values are given as mean (SEM).

	Group N $n=40$	Group H $n=30$	Group L $n=13$
Age, years	73.8 (1.0)	74.9 (1.2)	75.5 (2.1)
Range	60–85	61–89	63–88
Sex M/F	19/21	13/17	7/6
Weight, kg	69.3 (1.8)	67.4 (2.3)	69.8 (4.6)
Range	46–96	38–90	54–94
Duration of surgery, minutes	43.3 (2.0)	47.4 (1.7)	42.5 (1.0)
Range	20–75	30–65	40–45
$P\text{aCO}_2$, kPa	4.9 (0.7)	2.9 (0.6)	—
Range	4.0–7.0	2.3–3.9	
$P\text{aO}_2$, kPa	23.0 (9.8)	22.0 (5.9)	—
Range	12.5–48.0	12.2–28.6	
Fresh gas flow, litres/minute	4.7 (0.2)	13.8 (0.5)	—
Range	3.0–12.5	8.4–20.0	
FGF/weight, ml/minute/kg	67.3	205.4	—

Table 3. RBMT, the mean (SEM) combined scores.

	Test 1 Before operation	Test 2 After 4 days	Test 3 After 4 weeks
Group N	55.4 (1.2) $n=40$	54.3 (1.2) $n=39$	56.1 (1.2) $n=34$
Range	39.0–74.0	36.5–70.0	43.5–73.5
Group H	50.8 (1.5) $n=30$	49.2 (1.6) $n=29$	51.8 (1.4) $n=29$
Range	35.0–63.50	35.0–66.50	40.5–66.0
Group L	52.0 (1.7) $n=13$	58.0 (1.3) $n=13$	57.2 (1.8) $n=12$
Range	39.5–61.5	47.0–66.0	48.0–71.0

Psychometric testing was carried out in the pilot study in order to obtain familiarity and confidence with administration of these tests.

Results

Patients

Forty patients in Group N, 30 in Group H and 13 in Group L participated in the trial. A profile of these patients is given in Table 2.

Psychometric tests

Table 3 tabulates the mean combined scores of RBMT and Table 4 shows the mean RTs for each group before and after the operation.

One patient from Group N and one from Group H were discharged early and therefore did not perform the 4-day tests, although they did perform the 4-week tests. Eight patients, six from Group N, one from group H and one from Group L, either failed to keep their outpatients appointment or were unwilling to complete the 4-week tests. USRT test was not satisfactorily performed by 10 patients, five in Group N, four in Group H and one in Group L. One of these patients had severe contracture of the fingers and was therefore unable to press the button quickly. However, she successfully completed the RBMT, and hence was included in the study. One patient complained of headache and sore eyes through the effort of concentration, and four failed to learn the test. There were problems with the tape in the remaining four patients.

The data were statistically analysed using Wilcoxon matched-pairs signed-ranks test and Kruskal–Wallis one-way analysis of variance.

The mean combined RBMT scores were marginally lower in the 4-day test in both Groups N and H. The mean combined score was higher on the fourth day in the local

Table 4. USRT, the mean (SEM) time in msec.

	Test 1 Before operation	Test 2 After 4 days	Test 3 After 4 weeks
Group N	346.2 (10.1) $n=35$	347.1 (10.3) $n=34$	344.5 (11.9) $n=34$
Range	231.0–473.8	239.0–501.0	205.4–551.0
Group H	357.2 (10.2) $n=26$	360.8 (9.8) $n=26$	361.2 (13.1) $n=24$
Range	281.2–461.2	269.8–491.7	262.0–524.8
Group L	342.8 (16.1) $n=12$	339.2 (14.5) $n=12$	339.2 (19.7) $n=11$
Range	266.3–461.4	267.1–424.7	250.3–480.2

anaesthetic group. None of these changes reached statistical significance. There was a slight prolongation of reaction time in the 4-day test in Groups N and H compared to Group L in which the reaction time was faster. These were insignificant changes. The mean RBMT scores were higher in the 4-week test than the pre-operative scores in all three groups. Again, the increase was not significant. The mean RTs were shorter at 4 weeks than pre-operatively in Groups N and L. The RT was still prolonged at this time in Group H. These differences were not significant.

Discussion

Flatt *et al.*[9] acknowledged the difficulty of studying effects of anaesthesia on mental function due to a large number of variables that may affect postoperative performance. These factors are: characteristics of the surgery accompanying anaesthesia; events during anaesthesia such as hypotension, hypocarbia, and hypoxia; differences in the effects of anaesthetic agents; influences of different premedication agents; the effects of hospital environment on the motivation and wellbeing of patients; practice effects on repeated administrations of a particular test of mental function.

A considerable time was spent in the design of the present study to control some of these variables. All patients underwent the same surgical procedure, that is, cataract extraction with (or without) intra-ocular lens implantation. Hyperventilation of the lungs is often employed in these patients in order to reduce intra-ocular tension. The nature of surgery is such that, in itself, it imposes minimum physiological disturbance. Hypoxia was not detected either clinically or in any of the arterial blood gas samples. The systolic blood pressure was maintained within 10% of the baseline value through judicious use of enflurane. All patients, including those in the local anaesthetic group, received oral temazepam premedication. Temazepam has a short elimination half-life and possesses no long-acting metabolite. Thus it would have no effect on performance of psychometric tests 4 days after operation. All patients in the general anaesthesia groups received the same anaesthetic agents according to a standard protocol. The local anaesthetic group was included merely to allow for the effects of hospitalisation.

The present study employed the Rivermead Behavioural Memory Test to detect cerebral dysfunction. Both short- and long-term memory are adversely affected by cerebral insults. However, long-term memory is likely to be more susceptible to global insults such as hypoxia and anaesthesia.[22,23] The RBMT tests both short- and long-term recall. It has been used to detect memory loss after head injury, cerebrovascular accidents, and in senile and presenile dementia.[20] The tasks involved are analogues of a range of everyday situations which involve memory[20,25,26] and therefore, provide a more accurate reflection of patients' handicap for normal living.

Unprepared Simple Reaction Time test is a reliable test of arousal.[21] It is sensitive to the effects of stresses, like sleep deprivation, that normally influence arousal, yet it is a relatively short test. Also, it has a very short practice effect. Thus, it was ideally suited to the requirements of the present investigation.

Ten out of 83 patients failed to complete the USRT test satisfactorily. However, only four (4.8%) of these failures were due to inability to learn the test. This is perhaps not surprising in view of the mean age of the patients who formed this study group. Of the rest, the failure to record the reaction times on the cassette tape in four patients was due to low batteries and could have been prevented. The patient with contracture of the fingers successfully completed the RBMT and therefore was included in the study.

It is possible that a delay in reaction time can occur at any site in the neural pathways, but the most likely site is within the central nervous system.[7] The patient kept the finger close to the button on the reaction time device at all times and thus the motor component of the pathway was less likely to affect RT values. Twenty minutes of distributed practice of the test was recommended for the performance to reach asymptote.[21] However, it is considered that in order to maintain the concentration and cooperation of the elderly patients, the total duration of the test session should be kept under one hour. Therefore, it was decided that two 5-minute practice tests were an acceptable compromise.

The psychometric tests were performed 4 days and 4 weeks after the operation. It is a routine practice in this hospital to send patients home 4 days after cataract surgery. This is the time when they are out in the community and have to lead an independent life. Thus, the fourth postoperative day seemed an appropriate time to test them. The 4-week test was performed to assess any long-term deficit, since some of the investigators have shown that impairments last more than a few days.[7,9]

In conclusion, this study of elderly patients undergoing cataract surgery, who were ventilated to a mean $P\text{aCO}_2$ of 2.9 kPa for a mean period of 47.4 minutes showed no impairment of psychological function as measured by the Rivermead Behavioural Memory Test and Unprepared Simple Reaction Time test. The fact that both the memory and reaction time measures are consistent strengthens this conclusion.

Acknowledgments

This study was supported by the Research Grant no. 21 from the East Anglian Regional Health Authority and was based at the Ipswich Hospital, Heath Road, Ipswich.

The author wishes to thank Drs S.G. Harrison, M.H. Cook, D.J. Elliott, M.G. Smith and Professor A.P.Adams for their invaluable help; Messrs R.E. Lewis and I.D. Simpson for permission to study patients under their care; Drs A.D. Baddeley (Director), and R.T. Wilkinson (Head, Psychophysiology Section, MRC Applied Psychology Unit, Cambridge) for their expert psychological advice and guidance; and Miss S. Roberts (Senior Research Assistant, Department of Community Medicine, Medical Statistics and Computing Group, University of Cambridge, Cambridge) for her help with the statistical analysis. The author also gratefully acknowledges the cooperation of the nursing staff of Sproughton Ward and the Eye Clinic at The Ipswich Hospital, Ipswich.

References

1. Clutton-Brock J. The cerebral effects of overventilation. (Preliminary communication.) *British Journal of Anaesthesia* 1957; **29:** 111–3.
2. Wolff HG, Lennox WG. Cerebral circulation XII: Effect on pial vessels of variations in the oxygen and carbon dioxide

content of blood. *Archives of Neurology and Psychiatry* (Chicago) 1930; **23:** 1097–1120.

3. Kety SS, Schmidt CF. The effects of active and passive hyperventilation on cerebral blood flow, cerebral oxygen consumption, cardiac output, and blood pressure of normal young men. *Journal of Clinical Investigation* 1946; **25:** 107–19.
4. Lambertsen CJ, Kough RH, Cooper DY, Emmel GL, Loeschke HH, Schmidt CF. Oxygen toxicity. Effects in man of oxygen inhalation at 1 and 3.5 atmospheres upon blood gas transport, cerebral circulation and cerebral metabolism. *Journal of Applied Physiology* 1953; **5:** 471–86.
5. Allen GD, Morris LE. Central nervous system effects of hyperventilation during anaesthesia. *British Journal of Anaesthesia* 1962; **34:** 296–305.
6. Blundell E. A psychological study of the effects of surgery on eighty-six elderly patients. *British Journal of the Society of Clinical Psychologists* 1967; **6:** 297–303.
7. Wollman SB, Orkin LR. Postoperative human reaction time and hypocarbia during anaesthesia. *British Journal of Anaesthesia* 1968; **40:** 920–6.
8. Hovorka J. Carbon dioxide homeostasis and recovery after general anaesthesia. *Acta Anaesthesiologica Scandinavica* 1982; **26:** 498–504.
9. Flatt JR, Birrell PC, Hobbes A. Effects of anaesthesia on some aspects of mental functioning of surgical patients. *Anaesthesia and Intensive Care* 1984; **12:** 315–24.
10. Whitwam JG, Boettner RB, Gilger AP, Littell AS. Hyperventilation, brain damage and flicker. *British Journal of Anaesthesia* 1966; **38:** 846–52.
11. Blenkarn GD, Briggs G, Bell J, Sugioka K. Cognitive function after hypocapnic hyperventilation. *Anesthesiology* 1972; **37:** 381–6.
12. Murrin KR, Nagarajan TM. Hyperventilation and psychometric testing. A preliminary study. *Anaesthesia* 1974; **29:** 50–8.
13. Karhunen U, Jönn G. A comparison of memory function following local and general anaesthesia for extraction of senile cataract. *Acta Anaesthesiologica Scandinavica* 1982; **26:** 291–6.
14. Henville JD, Adams AP. The Bain anaesthetic system. An assessment during controlled ventilation. *Anaesthesia* 1976; **31:** 247–56.
15. Bain JA, Spoerel WE. Flow requirements for a modified Mapleson D system during controlled ventilation. *Canadian Anaesthetists' Society Journal* 1973; **20:** 629–36.
16. Rose DK, Froese AB. The regulation of $Pa\mathrm{CO}_2$ during controlled ventilation of children with a T-piece. *Canadian Anaesthetists' Society Journal* 1979; **26: 104–13.**
17. Nunn JF. Carbon dioxide In: Nunn JF. *Applied respiratory physiology*. London: Butterworths, 1977: 351.
18. Cronin M, Redfern PA, Utting JE. Psychometry and postoperative complaints in surgical patients. *British Journal of Anaesthesia* 1973; **45:** 879–86.
19. Gotoh F, Meyer JS, Takagi Y. Cerebral effects of hyperventilation in man. *Archives of Neurology* 1965; **12:** 410–23.
20. Drummond GB. The assessment of postoperative mental function. *British Journal of Anaesthesia* 1975; **47:** 130–42.
21. Wilson BA. Assessment for rehabilitation: the Rivermead Behavioural Memory Test. In: Wilson BA. *Rehabilitation of memory*. New York: The Guildford Press, 1987: 89–104.
22. Wilkinson RT, Houghton D. Field test of arousal: a portable reaction timer with data storage. *Human Factors* 1982; **24:** 487–93.
23. Crow TJ, Kelman, GR. Effect of mild acute hypoxia on human short-term memory. *British Journal of Anaesthesia* 1971; **43:** 548–52.
24. James FM. The effects of cyclopropane anesthesia without surgical operation on mental functions of normal man. *Anesthesiology* 1969; **30:** 264–72.
25. Eckenhoff JE, Compton JR, Larson A, Davies RM. Assessment of cerebral effects of deliberate hypotension by psychological measurements. *Lancet* 1964; **ii:** 711–4.
26. Sunderland A, Harris JE, Baddeley AD. Do laboratory tests predict everyday memory? A neuropsychological study. *Journal of Verbal Learning and Verbal Behavior* 1983; **22:** 341–57.
27. *The Rivermead Behavioural Memory Test manual.* Thames Valley Test Company, Reading. Published 1985.

Appendix

Rivermead Behavioural Memory Test[20,26]

This is a description of the subtests of RBMT in the order in which they are administered and the scoring method.

Items 1 and 2. Remembering a name

The subject is shown a photographic portrait and told the first and second name of the person in the photograph.

Item 3. Remembering a hidden belonging

A possession belonging to the subject (e.g. a pen or an appointment card) is borrowed and secreted (e.g. in a drawer or a cupboard). The subject is requested to ask for the belonging at the end of test session and to remember where it is hidden.

Item 4. Remembering an appointment

An alarm is shown to the subject and then set for 20 minutes. The subject is told to ask a particular question relating to the near future when the alarm rings. For example, the subject has to ask when his (her) next appointment is on hearing the alarm ring.

Item 5. Picture recognition

Line drawings of 10 common objects are shown, one at a time for 5 seconds each. The subject is required to name each picture and after a filled delay, to select the original 10 from a set of 20.

Item 6a. Immediate prose recall

The subject is asked to listen to a short passage of prose being read out and to remember as much of it as possible. She (he) has to recall as much of the story as she (he) can.

Score. Each parallel version of the story is divided into 21 details. One point is scored for each detail recalled word perfect, one point for a close synonym, 0.5 point for partially correct recall or approximate synonym.

Item 5. Picture recognition

The subject is now presented with 20 pictures comprising the 10 seen before and 10 new ones in prescribed order. She (he) is required to recognise the original 10 from 10 distractors. Presentation is unpaced but the subject is encouraged to guess if unsure.

Score. The number of false positives is deducted from the number of correct ones to obtain the total score.

Item 7. Face recognition

The subject is shown A7 size pictures of five faces, one at a time for 5 seconds each.

Item 8a. Remembering a short route

The tester traces a short route within the room. The route comprises five sections, e.g. a chair, door, window, table and return to chair. The subject is required to reproduce the route immediately.

Score. One point is scored for each stage on the route followed in the correct order.

Item 9a. Remembering to deliver a message

An envelope marked 'Message' is placed in a suitable place (e.g. on the table, chair or window) while tracing the route. The subject is required to pick up the envelope and leave it in the correct place.

Score. Two points are scored if the envelope is picked up spontaneously, one point if it is picked up after a reminder. One point is scored if the envelope is left in the correct place. Thus the subject can score a maximum of 3 points.

Item 7. Face recognition

The subject is presented with photographs of 10 faces, five of which are new. She (he) is required to recognise the original five faces from five distractors. Presentation is unpaced and subjects are encouraged to guess if necessary.

Score. The number of false positives is deducted from the number correct to obtain the total score.

Item 10 and 11. Orientation and date

The subject is asked 10 orientation questions as follows: (i) 'What year is it now?' (ii) 'What month is it?' (iii) 'What day of the week is it?' (iv) 'What date is it?' (v) 'What place are we in now?' (vi) 'What town are we in now?' (vii) 'How old are you now?' (viii) 'In what year were you born?' (ix) 'What is the name of the present Prime Minister of Britain?' (x) 'What is the name of the President of the USA?'

Score. The number correct is scored out of a total of 9. the date is scored separately. *Note:* The following tests are not begun until after the alarm has rung. The subject is engaged in conversastion if necessary.

Item 4. Remembering an appointment

At the sound of alarm ringing the subject is meant to ask the tester the specific question mentioned previously. She (he) is prompted if she (he) does not.

Score. Two points are scored if the subject asks the correct question spontaneously; if after a prompt, one point is given. No recall or incorrect recall scores no point. One point is scored if subject spontaneously remembers that something has to be asked but cannot remember what it is.

Item 6b. Delayed prose recall

The subject is now asked to recall the story which was previously read out to him (her).

Score. The same scoring procedure as for the immediate recall is employed.

Item 8b. Delayed recall of route

The subject is required to retrace the original route. Scoring is as for item 8a.

Item 9b. Remembering to deliver a message

The subject is stopped from tracing the route and prompted if she (he) fails to pick up the envelope spontaneously. Scoring is as for item 9a.

Items 1 and 2. Remembering a name

The original photograph is shown. The subject is required to recall the first and second names, if necessary after a first letter cue.

Score. Two points are given if first name is recalled without a prompt, one point if after a prompt. The scoring is repeated for the second name.

Item 3. Remembering a belonging

The subject is told that the test session has now ended. The tester waits for 5 seconds to see if the subject recalls where the object was hidden as well as its identity. If not, she (he) is prompted.

Score. The subject scores 2 or 0 for sections (i) and (ii), and 1 or 0 for sections (iii) and (iv). The sum gives the total score: (i) Remembered place without prompting; (ii) Remembered item without prompting; (iii) Remembered place after prompting; (iv) Remembered item after prompting.

Anaesthesia, 1989, Volume 44, pages 641–643

Anaesthesia and brain damage in the newborn

A. J. CHARLTON, J. M. DAVIES AND S. RIMMER

Summary

Eighty newborn babies were studied by ultrasound brain scan before and after their first general anaesthetic. Periventricular haemorrhage or ischaemia occurred in 23 patients (29%) and affected both term and premature babies. Four new lesions developed but only three of 19 existing lesions deteriorated. The very premature (< 33 weeks gestation) were most at risk (four of eight deteriorated). Deterioration or development of lesions occurred only in very ill babies with known risk factors. Anaesthesia did not appear to be implicated in any case.

Key words

Anaesthesia; paediatric.
Brain; haemorrhage, ischaemia.

The immature brain of the neonate is vulnerable both to periventricular haemorrhage (PVH) and periventricular ischaemic damage (PVL);[1] it is widely believed that anaesthesia may be a predisposing factor to PVH.[2,3] Typically, 48% of very premature babies (< 32 weeks gestation) in a medical intensive care unit develop PVH.[1] The majority of neonates who present for anaesthesia are full term, and no comparable data are available on such a population. PVH does occur in term babies, although rarely, but evidence of impaired autoregulation of cerebral blood flow after hypoxia[4] (which may occur at birth) suggests that they may also be at risk of ischaemic damage. Consequently, we have, whenever possible, incorporated cerebral ultrasound scans into the assessment of our patients. We report here on 80 babies examined by both pre- and postoperative brain scans. The aims of this preliminary study were to document the incidence of intracranial lesions, to assess whether development or deterioration of lesions occurred at a time which may relate to anaesthesia and finally to identify more precisely a study group for comparative investigation of anaesthetic techniques.

Methods

All patients were undergoing their first anaesthetic and were studied by real time ultrasound scans performed through the anterior fontanelle. The first 60 cases were examined using a Technicare Auto Sector Scanner with a 7.5 MHz probe and the remainder with an Acuson 128.

Two very experienced ultrasonographers (J.D. and S.R.) performed all the scans. Diagnostic criteria have been described previously.[1]

Every pre-operative scan was performed within 12 days of surgery (68 on the day of surgery or previous calendar day). Postoperative scans were performed between 4 hours and 17 days, 65 of them on the day of surgery or subsequent 3 days.

There were no clinical exclusion criteria; selection was determined by availability of personnel to perform the scans during office hours. A wide range of major surgical procedures was undertaken (Table 1). The study group included babies whose trachea was already intubated for intensive therapy before surgery. All patients underwent surgery during the first 33 days of life except one, with a previous PVH, who was still preterm but 72 days old. A range of anaesthetic techniques was employed, in accordance with the normal practice of five paediatric anaesthetists; the techniques were not altered by knowledge of scan findings.

Results

Eighty babies (25% of patient admissions) had both pre- and postoperative scans during a 2-year period. Abnormalities were reported in 23 cases (29%). Seven (9%) showed deterioration. None of these babies was more than 7 days old at the time of surgery. Four babies (5%) developed a lesion after a normal first scan; all had been

---

A.J. Charlton, MB, ChB, FFARCS, Consultant Paediatric Anaesthetist, J.M. Davies DCR(R), DMU, Superintendent Radiographer, S. Rimmer MB, ChB, DMRD, FRCR, Consultant Radiologist, North West Regional Neonatal Surgical Unit, St Mary's Hospital, Whitworth Park, Manchester M13 9WL.
Accepted 13 February 1989.

0003–2409/89/080641+03 $03.00/0 © 1989 The Association of Anaesthetists of Gt Britain and Ireland

Table 1. Operation type or main diagnosis.

	n
Laparotomy	33
Tracheo-oesophageal fistula	16
Diaphragmatic hernia	9
Exomphalos	5
Renal/bladder	3
Cystoscopy	2
Anoplasty	2
Testicular torsion	2
Sacrococcygeal teratoma	2
Cleft lip/palate	2
Central venous line	2
Cystic hygroma	1
Inguinal hernia	1

anaesthetised during the first 3 days of life. All the postoperative scans that showed an abnormality were recorded within 6 days of anaesthesia; all those that showed deterioration were performed within 5 days.

Postconceptual age at day of operation is shown in Table 2. Term babies were classified as those aged 37 weeks or more, premature babies 33 to 36 weeks, and the very premature 32 weeks or under.

Three types of lesion were encountered. Periventricular cysts located in the region of the germinal matrix were interpreted as the end result of antenatal PVH. Recent haemorrhages were graded in severity as 1 (subependymal), 2 (intraventricular) and 3 (parenchymal). The ischaemic lesions were of 'periventricular leucomalacia' (PVL) and occurred in isolation and in association with PVH (two cases). The distribution of lesions is shown in Table 3.

The seven babies whose scan deteriorated are described in Table 4 and the essentials of their anaesthetic management in Table 5.

There were 19 patients with lesions detected on first scan. Only three deteriorated; these were all very premature babies and tracheal intubation had been performed already for intensive care or resuscitation purposes. The remaining 16 did not deteriorate; in six of these, tracheal intubation was performed with the baby awake, in seven after thiopentone and muscle relaxant and in one after induction of anaesthesia with halothane.

All seven babies who showed deterioration had major clinical complications; the main details are shown in Table 6. Anaesthesia was complicated only in cases 5 (failure to intubate) and 4 (requirement for atropine and bicarbonate).

Discussion

Twenty-nine percent of our patients had ultrasound evidence of haemorrhagic or ischaemic brain injury during the peri-operative period. The majority of lesions were clinically silent and probably not associated with long-term major neurological damage. However, this high incidence justifies the anaesthetists' concern that their techniques should not contribute to these problems. We know of no published work which has demonstrated the widespread belief that anaesthesia may be harmful. The only reported study which attempted this demonstrated that 93 preterm babies showed no deterioration in PVH over the peri-anaesthetic period,[5] but the mean age of that study group was 15.6 days, outside the high risk time for PVH.[1,6]

Table 2. Number of patients who developed lesions or deteriorated, classified by postconceptual age group at day of operation.

	n	Lesion	Deterioration
Term	58	13	3
Premature	14	3	0
Very premature	8	7	4
	80	23	7

Table 3. Type of lesion by postconceptual age at operation.

	n	Cysts	Haemorrhage	Ischaemia
Term	13	3	1	9
Premature	3	0	2	1
Very premature	7	0	6	3

Our study appears to be the first to have shown peri-operative deterioration of neonatal intracranial lesions. However, this does not imply that anaesthesia is a contributory factor. It may be entirely coincidental. In one study, median onset of PVH in 219 very premature infants was at 2 days (range 1 to 4) and of ischaemic lesions at 7 days (range 1 to 70).[1] All cases of PVH in another study occurred within 72 hours of birth.[6] Sixty-two of our anaesthetics were given in the first 7 days of life, a timing which may simply have coincided with the natural development and evolution of lesions triggered by events before, at or after birth.

Postoperative events before the second scan may be implicated. This was believed to be particularly so in cases 2, 3 and 6. Among the many postnatal factors reported to be associated with development of PVH are intermittent positive pressure ventilation, continuous positive airways pressure, infant respiratory distress syndrome, hypercapnia, acidosis, administration of bicarbonate, rapid colloid infusion, blood pressure fluctuations, pneumothorax and hypothermia.[1,6,7] Birth asphyxia, recurrent apnoea, patent ductus arteriosus, septicaemia and seizures are associated with ischaemia.[1] All of the seven babies whose scan deteriorated had more than one of these features.

Specific areas of concern about anaesthetic techniques have been highlighted recently. It has been suggested that awake intubation may predispose to PVH because it produces arterial hypertension,[2,3] and raises anterior fontanelle pressure[8] (an indirect correlate of intracranial pressure). Our recent report of term babies which was based on

Table 4. Details of babies with deterioration of scan findings.

Case no.	Gestation (weeks)	Day(s) of life	Weight (kg)	Lesion		
				Scan I	Scan II	Interval
1	37	3	1.76	nil	I	1
2	37	2	2.23	nil	I	5
3	38	2	1.80	nil	I	3
4	26	1	0.92	nil	H_3	< 1
5	32	2	1.55	H_2+I	*H_2+I	2
6	25	7	0.82	H_2	H_3	1
7	32	6	1.80	I	H_1+I	2

Interval, days between surgery and second scan; H, haemorrhage, with grade (see text); I, ischaemia; *new contralateral haemorrhage.

Table 5. Anaesthetic technique and outcome for the seven babies with deterioration of scan findings.

	Tracheal intubation	Supplements	Postoperative IPPV	Outcome
1	Awake (B)	—	—	
2	Halothane	Halothane	+	Died
3	Thiopentone	—	+	
4	ITU	—	+	Died
5	Thiopentone (B)	Fentanyl	+	
6	ITU	—	+	Died
7	ITU	Fentanyl	+	

ITU denotes previous intubation in intensive care unit; B, temporary tracheal intubation for resuscitation at birth.

data collected from this head scan study found no hypertensive response[9] and work with premature babies has shown increases of 9[10] and 20%[6] in systolic pressure. Mean age in the latter study (of six babies only) was 16 days and systolic pressure increased only to 74 mmHg; it has been reported that a fluctuation of 100% is an antecedent of PVH.[9] Anterior fontanelle pressure has been shown to increase with awake intubation in preterm[6] and term[11] infants, but was not associated with development of PVH in either study. In the study by Stow *et al.*[11] the increase during awake intubation was no greater than that which occurred with normal crying. Only one of the seven babies who deteriorated in our study (case 1) was intubated awake for anaesthesia and his medical complications were sufficient to account for his lesion. Six cases with existing lesions underwent awake intubation. None deteriorated. Tracheal intubation for anaesthesia was not a significant factor associated with deterioration.

It has been suggested also that supplementation of nitrous oxide anaesthesia may be protective.[3,12] Supplements were given to three babies who deteriorated. No supplements were given to five babies with existing lesions who did not deteriorate and to one who did. Overall we have no evidence to support or condemn any particular technique of anaesthesia.

This preliminary study has indicated a high incidence of intracranial lesions in a neonatal surgical population of mixed gestational age, and shown that these problems are not confined to the very premature. A detailed discussion of the aetiology of intracranial lesions in relation to ante- and postnatal care is not within the scope of this report, but we see little reason from our data to believe that anaesthesia is a risk factor. No well baby developed a lesion. Only three of 19 babies whose susceptibility to intracranial damage was evidenced by an existing lesion deteriorated and no deterioration occurred in babies anaesthetised beyond the first week of life. The babies whose lesions developed or deteriorated were all seriously ill with multiple complications, many of which were known risk factors[1,9,10] and were adequate in themselves to explain the lesions. A study to compare anaesthetic techniques may be difficult to construct because of the rarity (9%) of perioperative deterioration and the likely presence in all these patients of multiple factors known to be associated with development of lesions in the absence of anaesthesia.

Table 6. Details of the seven babies whose scan deteriorated after anaesthesia.

1	Intra-uterine growth retardation. Birth asphyxia. Pre-operative hypoglycaemia and convulsions. Duodenal stenosis.
2	Major exomphalos including liver. Difficult primary closure. Septicaemia. Pneumonia.
3	Primary repair of oesophageal atresia and tracheo-oesophageal fistula (TOF). Trachea extubated after surgery. Collapsed due to haemothorax with arterial $P\text{CO}_2$ 14.0 kPa. Reintubated awake. Haemophilia.
4	VATER association of anomalies.[13] Severe infant respiratory distress syndrome (IRDS) but required emergency ligation of TOF on day one for adequate IPPV.
5	Antenatal bilateral Grade 2 PVH with PVL, TOF and imperforate anus. Unsuspected tracheal stenosis. Emergency tracheostomy, ligation of TOF and anoplasty. Body temperature decreased to 33.6°C during 6-hour surgery.
6	Twin. IRDS. Persistent fetal circulation. Renal failure. Disseminated intravascular coagulation. Multiple bowel perforations. Arterial $P\text{CO}_2$ 15.0 kPa after inappropriate postoperative morphine.
7	Congenital diaphragmatic hernia, IPPV with 100% O_2. Dopamine and tolazoline until fit for surgery on day 6.

References

1. Sinha SK, Davies JM, Sims DG, Chiswick ML. Relation between periventricular haemorrhage and ischaemic brain lesions diagnosed by ultrasound in very pre-term infants. *Lancet* 1985; **2:** 1154–6.
2. Editorial. Pain, anaesthesia, and babies. *Lancet* 1987; **2:** 543–4.
3. Berry FA, Gregory GA. Do premature infants require anesthesia for surgery? *Anesthesiology* 1987; **67:** 291–3.
4. Lou HC, Lassen NA, Friis-Hansen B. Impaired autoregulation of cerebral blood flow in the distressed newborn infant. *Journal of Pediatrics* 1979; **94:** 118–21.
5. Friesen RH, Honda AT, Thieme RE. Perianesthetic intracranial hemorrhage in preterm neonates. *Anesthesiology* 1987; **67:** 814–6.
6. McDonald MM, Koops BL, Johnson ML, Guggenheim MA, Rumack CM, Mitchell SA, Hathaway WE. Timing and antecedents of intracranial hemorrhage in the new born. *Pediatrics* 1984; **74:** 32–6.
7. Levene MI, Fawer CL, Lamont RF. Risk factors in the development of intraventricular haemorrhage in the preterm neonate. *Archives of Disease of Childhood* 1982; **57:** 410–7.
8. Friesen RH, Honda AT, Thieme RE. Changes in anterior fontanel pressure in preterm neonates during tracheal intubation. *Anesthesia and Analgesia* 1987; **66:** 874–8.
9. Charlton AJ, Greenhough SG. Blood pressure response of neonates to tracheal intubation. *Anaesthesia* 1988; **43:** 744–6.
10. Friesen RH, Henry DB. Cardiovascular changes in preterm neonates receiving isoflurane, halothane, fentanyl, and ketamine. *Anesthesiology* 1986; **64:** 238–42.
11. Stow PJ, McLeod ME, Burrows FA, Creighton RE. Anterior fontanelle pressure responses to tracheal intubation in the awake and anaesthetized infant. *British Journal of Anaesthesia* 1988; **60:** 167–70.
12. Anand KJS, Sippell WG, Aynsley-Green A. Randomised trial of fentanyl anaesthesia in preterm babies undergoing surgery: effects on the stress response. *Lancet* 1987; **1:** 243–8.
13. Quan L, Smith DW. The Vater association: vertebral defects, anal atresia, tracheo-esophageal fistula with esophageal atresia, radial dysplasia. *Birth Defects* 1972; **8:** 75–9.

Anaesthesia, 1989, Volume 44, pages 644–647

Opioid supplementation during propofol anaesthesia

The effects of fentanyl or alfentanil on propofol anaesthesia in daycase surgery

A. C. MOFFAT, A. W. MURRAY AND W. FITCH

Summary

Sixty patients of ASA grade 1 or 2 who presented for minor daycase gynaecological or urological procedures were randomly allocated to three groups. Group A received fentanyl 1 μg/kg and Group B alfentanil 5 μg/kg prior to induction. Group C received no pre-induction opioid. Anaesthesia was induced intravenously with propofol and maintained using nitrous oxide 67% in oxygen supplemented with 20-mg bolus doses of propofol as required. The pre-induction administration of fentanyl or alfentanil was not found significantly to affect either the doses of propofol required for induction or maintenance or the quality of anaesthesia compared with propofol alone. These results suggest that for minor outpatient procedures under general anaesthesia, the concomitant use of a short-acting opioid confers no benefits over propofol with nitrous oxide and oxygen alone.

Key words

Anaesthetics, intravenous; propofol.
Analgesics, narcotic; fentanyl, alfentanil.

Since 1926, when Lundy[1] introduced the concept of 'balanced anaesthesia', there has been a tendency to use separate agents to achieve each aspect of the 'triad' of anaesthesia, and thereby reduce the overall requirement for any one agent. The available drugs at that time, if used as sole anaesthetic agents, would have resulted in undesirable cardiorespiratory changes and a protracted recovery phase. It may be possible, with the agents now available, to produce 'general anaesthesia' with a single agent without the disadvantages outlined above.

An anaesthetic technique using a minimum number of agents is sought, with the increase in daycase surgery, which provides the essential elements of balanced anaesthesia combined with a rapid return to 'street fitness'. The ideal profile for a single anaesthetic agent includes a rapid onset of anaesthesia, short duration of action, lack of cumulation on repeated administration, an absence of excitatory effects during induction and recovery, and minimal postoperative sequelae. Propofol, since its introduction in 1986, has been shown to have many of these properties.[2,3] Previous studies have been performed to assess propofol both as a sole anaesthetic agent and in combination with fentanyl.[4,5] Since the introduction of alfentanil, studies have examined its use with propofol. However, there are no direct comparisons with this combination and that of fentanyl and propofol in daycase anaesthesia.

The present study was designed to establish whether propofol in combination with the short-acting opioids, fentanyl or alfentanil, provides a better quality of anaesthesia than propofol alone, and in addition to assess any differences between the opioid groups.

Methods

Hospital Ethics Committee approval was given for the study and written informed consent obtained from 60 patients aged 18 to 55 years of ASA grade 1 or 2. These patients were scheduled, as day cases, to have either minor gynaecological procedures such as dilatation and curettage, termination of pregnancy, or urological procedures such as cystoscopy, vasectomy, testicular biopsy. Patients were not studied if they had significant respiratory, cardiovascular, hepatic, renal, haemopoietic or endocrine disorders, or if they were pregnant or potentially pregnant, unless this was to be terminated as part of the procedure. Patients with previous adverse reactions during general anaesthesia, with a history of allergy to the trial drug or its constituents, or receiving medication likely to influence the course of anaes-

---

A.C. Moffat, FFARCSI, A.W. Murray, FFARCS, Anaesthetic Registrars, W. Fitch, BSc, PhD, FFARCS, Professor, University of Glasgow, University Department of Anaesthesia, Queen Elizabeth Building, Royal Infirmary, 8–16 Alexander Parade, Glasgow G31–2ER.

Accepted 15 January 1989.

0003–2409/89/080644+04 $03.00/0 © 1989 The Association of Anaesthetists of Gt Britain and Ireland

thesia (i.e. tranquillisers, neuroleptics or other psychoactive drugs), or who were grossly obese with their body weight greater than 20% in relation to normal for their height were also not studied.

Premedication was omitted and patients were randomly allocated to one of three groups in a blind manner. Thereafter the study became open. Group A received fentanyl 1 μg/kg 3 minutes before induction of anaesthesia; Group B received alfentanil 5 μg/kg one minute before induction. Group C received no pre-induction analgesic supplements. Lignocaine 10 mg was injected intravenously via a vein on the dorsum of the hand immediately prior to the injection of propofol. To allow the influence of the analgesic on the dose requirement of propofol to be examined, an initial dose of 1.5 mg/kg was given intravenously over a period of 20 seconds, with supplementary doses as required to complete induction. All patients were allowed to breathe spontaneously. Anaesthesia was maintained with a mixture of 67% nitrous oxide in oxygen, and bolus doses of 20 mg of propofol were given if the patient responded to surgical stimulation by moving. Analgesic supplements were given if the patient showed signs of inadequate analgesia, such as a 25% increase in arterial blood pressure or heart rate above baseline values, hyperventilation or lacrimation. Patients in Groups A and C received fentanyl 0.5 μg/kg and those in group B alfentanil 2.5 μg/kg.

Heart rate was recorded continuously from an ECG monitor and arterial pressure measured using a Datascope Accutorr 2 noninvasive blood pressure monitor. Recordings were made before drugs were given, 2 minutes after induction and at 5-minute intervals thereafter.

The induction dose and the timing of maintenance boluses were noted during anaesthesia. The administration of any analgesic supplements was recorded. Assessment of the quality of anaesthesia and the occurrence of any unwanted effects such as movement, apnoea, laryngospasm and hiccup were noted throughout this period.

Induction time was taken as the interval from the beginning of injection of propofol until the patient stopped counting. The anaesthetic time was taken as the interval from start of injection of induction agent until the end of surgery. The recovery time was from the end of surgery until the patient was able to open eyes and give the correct date of birth.

The requirements for analgesics and antiemetics were noted during recovery. Quality of recovery was assessed and note made of the occurrence of euphoria, depression, confusion or coughing. The patients were asked about awareness during anaesthesia and their satisfaction with the technique.

Results

Sixty patients entered the study; one patient in Group C was withdrawn because laryngeal spasm developed at induction, which was not relieved by additional doses of propofol. This led to the abandonment of the protocol.

Table 1 shows the characteristics of the three groups in terms of age, weight and sex. There were no significant differences between them. Table 2 compares the induction doses, maintenance rates and intra-operative analgesic requirements. All patients required additional propofol after induction to maintain anaesthesia. This ranged from one to 19 supplements. Four patients in Group A, one in Group B and four in Group C required analgesic supplements during the procedure. Differences between the groups were not significant. The induction times, duration of anaesthesia and recovery times are shown in Table 3. No differences were found between the three groups for these variables.

Table 4 gives a subjective assessment of the quality of anaesthesia. Of the 59 patients, only one from Group A and one from Group C had apnoea that lasted longer than 60 seconds. There were no major adverse reactions, and side effects were minimal in all groups. The frequency of the occurrence of any unwanted effects during the recovery period is shown in Table 5. No patients complained of awareness during the procedure when they were visited after operation. None of the patients was nauseated or required any antiemetic therapy. Oral analgesics were required by three patients in Group A, three in Group B and four in Group C. All patients were satisfied with their management and would be happy to have the same anaesthetic again.

Table 1. Details of patients. Values expressed as mean (SD).

	Group A (fentanyl) ($n=21$)	Group B (alfentanil) ($n=20$)	Group C (nil) ($n=18$)
Age, years	32 (11)	37 (11)	35 (11)
Weight, kg	65.1 (11.5)	64.7 (13.5)	62.6 (8.0)
Male:female ratio	10:11	8:12	5:13

There was no significant difference between groups (Student's *t*-test).

Table 2. Induction doses, maintenance rates, number of propofol supplements and intra-operative analgesic requirements. Values expressed as mean (SD).

	Group A (fentanyl) ($n=21$)	Group B (alfentanil) ($n=20$)	Group C (nil) ($n=18$)
Induction dose, mg/kg	2.67 (0.51)	2.42 (0.37)	2.68 (0.47)
Total maintenance dose, mg	129 (83.8)	115 (82.0)	124 (56.4)
Maintenance rate, mg/kg/minute	0.11 (0.04)	0.11 (0.035)	0.12 (0.049)
Number of propofol supplements (range)	6.4 (1–17)	5.6 (1–19)	6.2 (2–11)
Number of patients who received analgesic supplements	4	1	4

There was no significant difference between groups (Student's *t*-test).

Table 3. Induction times, duration of anaesthesia and recovery times. Values expressed as mean (SD).

	Group A (fentanyl) ($n=21$)	Group B (alfentanil) ($n=20$)	Group C (nil) ($n=18$)
Induction time, seconds	45 (20)	48 (16)	47 (13)
Duration of anaesthesia, minutes	13.1 (6.3)	11.8 (5.2)	11.2 (3.1)
Recovery time, minutes	5.7 (1.7)	5.4 (2.0)	5.8 (1.6)

There was no significant difference between groups (Student's *t*-test).

Table 4. Subjective assessment of quality of anaesthesia.

	Group A (fentanyl) ($n=21$)	Group B (alfentanil) ($n=20$)	Group C (nil) ($n=18$)
Quality of induction			
Good	17	18	14
Adequate	3	2	3
Poor	1	0	1
Abandonment of protocol	0	0	1
Apnoea after induction (>30 seconds)	6	4	2
Movement during procedure			
None	14	17	12
Slight	4	1	3
Moderate	3	2	3
Control of depth of anaesthesia			
Good	20	19	14
Adequate	1	1	4

No significant differences between the groups (Mann–Whitney *U* test).

Table 5. Side effects during the recovery period.

	Group A (fentanyl) ($n=21$)	Group B alfentanil) ($n=20$)	Group C (nil) ($n=18$)
Cough	—	—	1
Bronchospasm	—	—	—
Flush/rash	—	—	—
Headache	—	—	—
Nausea	—	—	—
Vomiting	—	—	—
Elation/euphoria	—	1	—
Depression/crying	1	—	1
Confusion	1	—	1
Intra-operative awareness	—	—	—
Number of patients who required postoperative analgesia	3	3	3

The cardiovascular changes from baseline to 5 minutes after induction are compared in Table 6. The mean arterial pressures were found to decrease in all three groups but there were no significant differences between the groups. The changes in heart rates were less uniform than those in the arterial pressure and a significant difference was found between Group A and Group B at the 5% level (Fig. 1).

Discussion

This study was designed to assess whether pretreatment with a short-acting opioid confers any benefits in terms of quality of anaesthesia or reduction in propofol requirements over propofol alone for minor outpatient procedures. The results indicate that the pre-induction administration of either fentanyl 1 μg/kg or alfentanil 5 μg/kg did not significantly affect the induction dose or maintenance requirements of propofol. Quality of induction and control of the depth of anaesthesia were similar in all three groups and were judged to be good overall. The incidence of miscellaneous side effects during the recovery period was 7.5%. These side effects were minor and were acceptable by the patients. The cardiovascular changes were similar in all groups and were not clinically significant. This is in agreement with results found by Spiss *et al.*[6] They compared the haemodynamic effects of fentanyl and alfentanil when administered in combination with etomidate for induction of anaesthesia in patients undergoing cardiac surgery. However a study by Van Aken *et al.*[4] showed a significantly greater decrease in arterial blood pressure in a group given fentanyl 3 μg/kg prior to an induction bolus of propofol 2.5 mg/kg. No such difference was found in our study. This could be explained by the use of a smaller and more appropriate dose of fentanyl and by titrating the propofol at induction to effect.

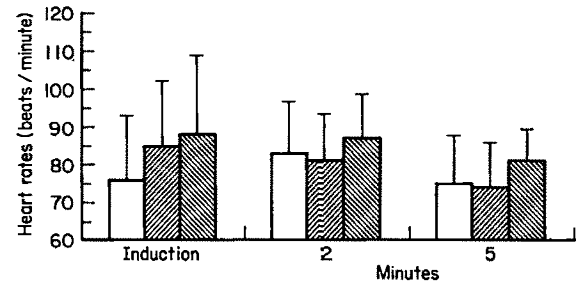


Fig. 1. Heart rate changes from induction to 2 and 5 minutes after induction. $p < 0.05$, significant difference in heart rate changes from induction to 5 minutes between Groups A and B (Student's *t*-test). □, Group A; ▨, Group B; ▧, Group C.

Certain patients were excluded on grounds of age, weight, co-existing pathology or current drug administration in order to standardise the groups as much as possible since all of these are known to influence drug requirements.[7-9] The patients were then allocated randomly in a blind fashion to the different groups. The study then became open although the results were not thought to be significantly influenced, since the recordings taken were of

Table 6. Blood pressure and heart rate changes. Values expressed as mean (SD).

	Group A (fentanyl) ($n=21$)	Group B (alfentanil) ($n=20$)	Group C (nil) ($n=18$)
Blood pressures, mmHg			
Induction			
Systolic	127 (26.4)	129 (25.1)	123 (19.8)
Diastolic	76 (17.1)	80 (12.1)	73 (15.3)
Mean	93 (19.4)	96 (15.3)	90 (15.5)
2 minutes			
Systolic	104 (21.6)	102 (14.5)	102 (18.5)
Diastolic	61 (13.0)	62 (12.1)	61 (14.5)
Mean	75 (14.8)	75 (12.1)	75 (14.8)
5 minutes			
Systolic	111 (19.4)	103 (14.4)	107 (17.6)
Diastolic	71 (14.9)	64 (9.3)	70 (13.4)
Mean	84 (16.2)	77 (10.7)	82 (14.3)
Heart rates, beats/minute			
Induction	76 (17.2)	85 (17.2)	88 (21.5)
2 minutes	83 (13.5)	81 (12.3)	87 (11.7)
5 minutes	75 (12.6)	74 (11.7)	81 (8.2)

$p<0.05$, significant difference in heart rate changes from induction to 5 minutes between Groups A and B. There was no significant difference in blood pressure changes. (Student's *t*-test.)

defined end-points such as the time of induction, duration of anaesthesia and recovery time or the presence or absence of particular side effects. However, it must be acknowledged that the study was not double-blind and this could have affected the results.

Previous studies have shown a difference in dose requirements of propofol after the administration of fentanyl.[5] The dose of opioid used, however, was fixed, irrespective of body weight, and the time from opioid pretreatment to induction was not standardised. The dosage of pre-induction opioid in this study was given based on the patients' weight and in accordance with the manufacturer's dosage recommendations for spontaneously breathing patients, to minimise any effect of what could otherwise be a considerable dose variation between patients. In addition to this, more appropriate timing of the pre-induction opiate injection may help to explain why there are no clinically significant differences between the fentanyl and alfentanil groups. Higher blood concentrations of propofol were found after pretreatment with fentanyl in a study by Cockshott *et al.*[10] They predicted from this that a smaller dose of propofol would be necessary to achieve a given depth of anaesthesia in patients pretreated with fentanyl. This has not been supported by our findings. In our study, as in others,[5,10,11] nitrous oxide was used as part of the anaesthetic technique. The analgesic properties of nitrous oxide are well known. In order to eliminate the influence this has on the intraoperative analgesic requirements, it would be necessary to repeat the study excluding nitrous oxide from the anaesthetic.

Few statistically significant differences were found between the groups in our study, but there were some trends that included less movement, better control of the depth of anaesthesia and somewhat lower maintenance rates in the opiate groups. This concurs with the results of a study by Millar and Jewkes,[12] who found that alfentanil improved the anaesthetic conditions but did not reduce propofol requirements significantly. Compared with a multicentre trial on propofol anaesthesia[11] the incidence of side effects during the recovery period in this study is lower. This may be related to the wider variation in observer bias associated with these larger trials.

Four patients in the nonopioid group received an analgesic supplement during the procedure. However, this was not statistically different from the number of patients in the opioid groups who received additional analgesia. We conclude from these results that propofol is satisfactory when used as a sole anaesthetic agent for daycase anaesthesia and that the pre-induction administration of a short-acting opioid confers no significant benefit.

Acknowledgments

We thank surgical and nursing staff from theatre and day stay wards for their cooperation and ICI Pharmaceuticals for their advice and funding of this study.

References

1. Lundy JS. Balanced anesthesia. *Minnesota Medicine* 1926; **9:** 299.
2. Cockshott ID. Propofol ('Diprivan') pharmacokinetics and metabolism—an overview. *Postgraduate Medical Journal* 1985; **61** (Suppl. 3): 45–50.
3. Grant IS, Mackenzie N. Recovery following propofol ('Diprivan') anaesthesia—a review of three different anaesthetic techniques. *Postgraduate Medical Journal* 1985; **61** (Suppl. 3): 133–7.
4. Van Aken H, Meinshausen E, Prien T, Brussel T, Heinecke A, Lawin P. The influence of fentanyl and tracheal intubation on the hemodynamic effects of anesthesia induction with propofol/N_2O in humans. *Anesthesiology* 1988; **68:** 157–63.
5. Thomas VL, Sutton DN, Saunders DA. The effect of fentanyl on propofol requirements for day case anaesthesia. *Anaesthesia* 1988; **3** (Suppl.): 73–5.
6. Spiss CK, Coraim F, Haider W, White PF. Haemodynamic effects of fentanyl or alfentanil as adjuvants to etomidate for induction of anaesthesia in cardiac patients. *Acta Anaesthesiologica Scandinavica* 1984; **28:** 554–6.
7. McCollum JSC, Dundee JW, Halliday NJ, Clarke RSJ. Dose response studies with propofol ('Diprivan') in unpremedicated patients. *Postgraduate Medical Journal* 1985; **61** (Suppl. 3): 85–7.
8. Patrick MR, Blair IJ, Feneck RO, Sebel PS. A comparison of the haemodynamic effects of propofol ('Diprivan') and thiopentone in patients with coronary artery disease. *Postgraduate Medical Journal* 1985; **61** (Suppl. 3): 23–7.
9. Redfern N, Stafford MA, Brooker J, Hull CJ. Incremental propofol for minor gynaecological procedures. *Postgraduate Medical Journal* 1985; **61** (Suppl. 3): 127.
10. Cockshott ID, Briggs LP, Douglas EJ, White M. Pharmacokinetics of propofol in female patients. Studies using single bolus injections. *British Journal of Anaesthesia* 1987; **59:** 1103–10.
11. Sanderson JH, Blades JF. Multicentre study of propofol in day case surgery. *Anaesthesia* 1988; **43** (Suppl.): 70–3.
12. Millar JM, Jewkes CF. Recovery and morbidity after day case anaesthesia. A comparison of propofol with thiopentone–enflurane with and without alfentanil. *Anaesthesia* 1988; **43:** 738–43.

Anaesthesia, 1989, Volume 44, pages 648–650

A clinical study into the possible intrinsic bradycardic activity of vecuronium

D. A. COZANITIS AND O. ERKOLA

Summary

Forty female patients received a standardised anaesthetic technique with thiopentone sodium and enflurane. Half of the patients received, under double-blind conditions, either physiological saline or glycopyrronium before induction of anaesthesia; 10 minutes after induction of anaesthesia, all patients received vecuronium 0.1 mg/kg. A further 10 patients received neither glycopyrronium nor vecuronium. The results show that vecuronium per se does not produce a decrease in heart rate.

Key words

Neuromuscular relaxants; vecuronium.
Heart; arrhythmia, bradycardia.

Vecuronium was introduced into clinical anaesthesia in the belief that it was free from cardiovascular activity.[1,2] However, anecdotal reports of bradycardia associated with the use of this non-depolarising neuromuscular blocking drug have appeared in the literature.[3,4] A controlled study revealed that a greater incidence of bradycardia occurred in patients who received vecuronium than in patients given pancuronium (a muscle relaxant with intrinsic vagolytic action) or vecuronium together with the anticholinergic drug glycopyrronium.[5] In that study, fentanyl, which has strong parasympathomimetic activity,[6] and surgery of a nature that might have provoked vagal stimulation, may have influenced the results. A further study was conducted in which these two factors were eliminated.[7] The incidence of bradycardia was less than that in the first study,[5] but the patients who received vecuronium showed a greater tendency towards bradycardia than did a group given atracurium, an agent which is also reported to be free from cardiovascular activity.[4] The present study was designed to determine whether vecuronium possesses intrinsic bradycardic activity.

Patients and methods

Forty females aged between 30 and 55 years, with a maximum weight of 75 kg and scheduled to undergo elective hysterectomy, entered the study. They were seen by the anaesthetist on the day before surgery and consent was obtained. The patients were given chlordiazepoxide 10 mg tablets in two divided doses, and at night all received nitrazepam 7.5 mg orally. None was receiving any medication known to affect heart rate, and the 12-lead electrocardiograph (ECG) was normal in all cases. This ECG was used to derive the heart rate on the day of admission. Heart rate and arterial pressure were recorded at the pre-anaesthetic visit. All patients were given oxycodone 0.14 mg/kg (maximum 10 mg) intramuscularly and diazepam 5 mg orally between 45 and 60 minutes before induction of anaesthesia. ECG electrodes (lead II) were applied in the operating room, and an intravenous infusion of Ringer's solution, into which the drugs were administered, was started.

Heart rate and arterial pressure were measured and recorded using an oscillotonometer. After a period of oxygenation, the patients received alcuronium 0.03 mg/kg followed by equal volumes of either physiological saline or glycopyrronium in a double-blind fashion, from coded ampoules. The dose of glycopyrronium was related to body weight as follows: < 59 kg, 0.20 mg; 60 to 75 kg, 0.25 mg. Thiopentone sodium 5 mg/kg was injected and on loss of the eyelash reflex, suxamethonium 1.5 mg/kg was given to facilitate tracheal intubation. The lungs were ventilated to normocapnia with oxygen/nitrous oxide (30/70%) and enflurane, initially at an inspired concentration of 2%; this was reduced to 0.7% within 3 minutes. Inspiratory and expiratory enflurane concentrations were monitored with a Normac Multigas Monitor (Datex). Heart rate was recorded just before induction of anaesthesia, after 10 minutes of enflurane anaesthesia (at which time vecuronium 0.1 mg/kg was injected) and thereafter at 1, 2, 3, 4, 5,

---

D.A. Cozanitis, BPharm, MB, ChB, MD, Surgical Hospital, O. Erkola, MD, Women's Clinic, Helsinki University Central Hospital, Kasarminkatu 11, SF 00130 Helsinki, Finland.
Accepted 27 February 1989.

0003–2409/89/080648+03 $03.00/0 © 1989 The Association of Anaesthetists of Gt Britain and Ireland

10 and 15 minutes. Arterial pressure was recorded before induction and at 10 and 15 minutes after vecuronium. Fifteen minutes after the injection of vecuronium those patients who had received glycopyrronium were given physiological saline, while those given saline received glycopyrronium 0.2 mg. In this way, all patients received glycopyrronium before the start of surgery, as is the standard practice here. Thereafter, fentanyl 0.1 mg was given and the scheduled surgery begun.

To exclude the possible influence of enflurane anaesthesia on heart rate[8,9] a further 10 patients were studied in a similar manner to the other two groups, except that neither glycopyrronium nor vecuronium was administered until the end of the study period, i.e. just before the start of surgery. An equal volume of saline was given in place of the anticholinergic and the relaxant.

Data were analysed using analysis of variance for repeated measurements and a two sample *t*-test.

Results

The groups of patients were similar demographically (Table 1). Ten minutes after the introduction of enflurane anaesthesia, the mean (SD) expired concentrations of enflurane in the glycopyrronium, saline, and control groups were 0.51 (0.04), 0.49 (0.03) and 0.49 (0.03) percent respectively.

Figure 1 shows the mean heart rates at the various assessment times. The patients were monitored for a further 15 minutes after the administration of vecuronium, i.e. a total exposure time to enflurane of 25 minutes. The data show that a mean decrease in heart rate of 10 beats/minute occurred during the 15-minute observation period in patients who did not receive vecuronium. The mean decreases in heart rate were 11 and 9 beats/minute respectively in the patients who received vecuronium after saline and those given vecuronium after glycopyrronium. Bradycardia, defined as a heart rate of less than 45 beats/minute, did not occur in any of the study individuals. Patients who received glycopyrronium had significantly higher heart rates throughout the study period than those who received saline ($p < 0.05$ to $p < 0.01$). Systolic arterial pressure was, on average, 5 mmHg greater in the glycopyrronium group.

Discussion

For practical reasons the patients were receiving enflurane for only 10 minutes before the injection of vecuronium; however, the mean expiratory concentration was similar at that time for the three study groups.

The results from this investigation indicate clearly that under the study conditions vecuronium does not decrease heart rate, i.e. it does not possess intrinsic bradycardic activity. Salmenpera *et al.*[10] suggested that vecuronium possesses such an action. However, their patients were all undergoing coronary bypass surgery and consequently received a wide range of cardioactive agents. Robertson *et al.*[11] found a statistically significant decrease in heart rate, albeit clinically insignificant, after the administration of vecuronium in an anaesthetic technique that involved the use of fentanyl. Inoue *et al.*[12] stated that vecuronium has a bradycardic effect which is particularly apparent in patients given fentanyl and (or) etomidate.

Table 1. Demographic details of the groups. Data are expressed as mean (SD).

	Saline	Glycopyrronium	Control
n	20	20	10
Age, years	41 (6)	39 (5)	38 (6)
Weight, kg	59 (7)	63 (7)	59 (7)
Height, cm	163 (7)	165 (6)	165 (5)

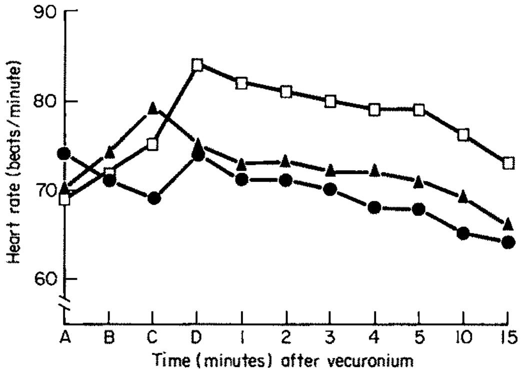


Fig. 1. Mean heart rate (beats/minute) in the three groups during the various study intervals. A, on admission; B, pre-anaesthetic visit; C, before induction; D, 10 minutes after enflurane. ●—●, control; ▲—▲, saline; □—□, glycopyrronium.

Bradycardia during anaesthesia can be multifactorial in origin. Drugs, surgical stimuli and disturbances to autonomic balance may result, alone or in combination, in a slowing of the heart rate. In the present study, a homogeneous population in respect of gender, age, weight and height was employed and all patients had a healthy cardiovascular status.

In addition, surgical stimuli were avoided until the completion of the study. The administration of vecuronium under these conditions, did not result in a greater decrease in heart rate than that associated with enflurane administration.

Acknowledgments

We acknowledge the patience of our gynaecological surgical colleagues, and the assistance of our anaesthesia nurses. A. H. Robins provided the clinical study supplies; we particularly thank C. J. Jones, BPharm, MRPharmS, and V. L. Pooley of that company.

References

1. Booij LHDJ, Edwards RP, Sohn YJ, Miller RD. Cardiovascular and neuromuscular effects of Org NC45, pancuronium, metocurine, and d-tubocurarine in dogs. *Anesthesia and Analgesia* 1980; **59:** 26–30.
2. Krieg N, Crul JF, Booij LHDJ. Relative potency of Org NC45, pancuronium, alcuronium and tubocurarine in anaesthetized man. *British Journal of Anaesthesia* 1980; **52:** 783–8.
3. Carter ML. Bradycardia after the use of atracurium. *British Medical Journal* 1983; **287:** 247–8.
4. Milligan KR, Beers HT. Vecuronium-associated cardiac arrest. *Anaesthesia* 1985; **40:** 385.
5. Cozanitis DA, Pouttu J, Rosenberg P. Bradycardia associated with the use of vecuronium. A comparative study with pancuronium with and without glycopyrronium. *Anaesthesia* 1987; **42:** 192–4.

P. 24 597

6. Marshall B, Wollman H. General anesthetics. In: Gilman AG, Goodman LS, Gilman A, eds. *The pharmacological basis of therapeutics,* 6th edn. New York: Macmillan, 1980: 295.
7. Cozanitis DA, Lindgren L, Rosenberg P. Bradycardia in patients receiving atracurium or vecuronium in conditions of low vagal stimulation. *Anaesthesia* 1989; **44:** 303–5.
8. Black GW. Enflurane. *British Journal of Anaesthesia* 1979; **51:** 627–40.
9. Gregoretti SM, Sohn YJ, Sia RL. Heart rate and blood pressure changes after Org NC45 (vecuronium) and pancuronium during halothane and enflurane anesthesia. *Anesthesiology* 1982; **56:** 392–5.
10. Salmenpera M, Peltola K, Takkunen O, Heinonen J. Cardiovascular effects of pancuronium and vecuronium during high-dose fentanyl anesthesia. *Anesthesia and Analgesia* 1983; **62:** 1059–64.
11. Robertson EN, Booij LHDJ, Fragen RJ, Crul JF. Clinical comparison of atracurium and vecuronium (Org NC45) *British Journal of Anaesthesia* 1983; **55:** 125–9.
12. Inoue K, El-Banayosy A, Stolarski L, Reichelt W. Vecuronium induced bradycardia following induction of anaesthesia with etomidate or thiopentone, with or without fentanyl. *British Journal of Anaesthesia* 1988; **60:** 10–7.

Anaesthesia, 1989, Volume 44, pages 651–655

Comparison of anxiety before induction of anaesthesia in the anaesthetic room or operating theatre

J. C. SONI AND D. A. THOMAS

Summary

Anxiety before induction of anaesthesia was studied in 100 patients who were allocated randomly to one of two groups. Patients in one group were anaesthetised in an anaesthetic room and those in the other group were anaesthetised inside the operating theatre. Both subjective and objective indices of anxiety were used in the comparison. Other factors that contributed to anxiety were assessed by a simple questionnaire. There was no significant difference in the level of anxiety between the two groups. The site of induction did not emerge as a major contributory factor to anxiety. The advantages and disadvantages of anaesthetic rooms are discussed.

Key words

Induction; anaesthesia.
Complications; anxiety.

Anaesthetic rooms have been a traditional feature of the operating theatre suite in the United Kingdom and are used routinely for the induction of anaesthesia. However, their use is not universal and in many countries induction of anaesthesia is carried out inside the operating theatre with no apparent disadvantages and probably with many advantages.[1]

Arguments in favour of anaesthetic rooms include the supposed reduction of fear by separation of the patient from the sights and sounds of the operating theatre,[2,3] the provision of a convenient place for the storage of equipment,[3] and a reduction in the delay between operations because the next patient may be anaesthetised while the previous operation is being completed,[3,4] especially if regional analgesia is to be used. Inhalational induction of anaesthesia in children also requires a quiet environment.

Disadvantages of anaesthetic rooms include inadequacy of monitoring vital functions during induction unless expensive equipment is duplicated, hazards associated with the transfer of the unconscious patient to the operating table and probably the cost of construction and maintenance of anaesthetic rooms and their equipment.

Opinion in the UK has been fairly unanimous that patients feel greater anxiety when anaesthetised inside the operating theatre. However, the authors are not aware of any published work to substantiate this view. Attempts have been made to improve the ambience of anaesthetic rooms by improved design, decor and lighting with a view to reduction of anxiety.[5-7] One of the authors (J.C.S.) whilst working in Holland in theatre suites without anaesthetic rooms appreciated the benefits of continuous monitoring during induction and found good patient acceptance. This has prompted the present study which was designed to assess and compare the level of anxiety before induction of anaesthesia in the anaesthetic room or the operating theatre and to evaluate other factors that contribute to anxiety in the peri-operative period.

Methods

This study was approved by the hospital ethics committee.

One hundred patients (50 males, 50 females) of ASA grade 1 or 2 and aged between 17 and 62 years were admitted to the study. They were scheduled for elective minor or intermediate operations in general, orthopaedic or ENT surgery. Patients were excluded if there was a past history of psychiatric illness, prescription of psychotropic drugs, antihypertensive drugs or β-blockers, or if they were scheduled for potentially cancer-related operations or daycase surgery. The patients were allocated randomly into two equal groups; induction of anaesthesia took place in the anaesthetic room in Group A and inside the operating theatre in Group B. There were equal numbers of male and female patients in each group. Random allocation was made by the theatre receptionist on arrival in the operating suite so that neither patient nor observer had prior knowledge of the group.

J.C. Soni, MB, BS, FFARCSI, Registrar, D.A. Thomas, FFARCS, Consultant, Department of Anaesthetics, Harold Wood Hospital, Gubbins Lane, Romford, Essex RM3 0BE.

Accepted 23 Feburary 1989.

0003–2409/89/080651+05 $03.00/0 © 1989 The Association of Anaesthetists of Gt Britain and Ireland

Table 1. Patient data. Values expressed as mean (SD).

	Group A (anaesthetic room) ($n = 50$)	Group B (theatre) ($n = 50$)
Age, years	37.1 (14.0)	36.3 (12.4)
Weight, kg	71.3 (15.9)	71.9 (10.5)
Sex, M : F	25:25	25:25
ASA status 1	50	46
ASA status 2	0	4
No. of previous operations		
None	14	14
One	22	18
Two	6	10
Three	7	4
Four	1	4

Quantitative measurement of anxiety was carried out subjectively by the use of the linear analogue anxiety scale in the form of a 10-cm horizontal line which was marked at one end 'No anxiety' and at the other end 'Extremely anxious'. The patient's heart rate (HR), systolic arterial pressure (SAP) and respiratory rate (RR) were used as objective indices of anxiety.

Each patient was visited before operation by one author (J.C.S.), in most cases on the day before the procedure. Informed consent was obtained, the use of the linear analogue anxiety scale explained and age, sex and weight were noted. Baseline readings of HR, SAP, RR and linear analogue anxiety score (LAAS) were taken. A note was made of the number of previous operations undergone by the patient. Premedication comprised oral temazepam (10 mg up to 60 kg body weight, 20 mg from 60 to 80 kg and 30 mg above 80 kg) approximately one hour before operation.

Care was taken to minimise the waiting period in the theatre suite but despite this there were some delays of 10–15 minutes, and one of 143 minutes. The patient was moved into the allocated site immediately before induction; those in Group A were taken into the anaesthetic room and those in Group B directly into theatre. All three theatres and anaesthetic rooms used in the study were identical in size, appearance, lighting and decor so that standard environmental conditions were ensured. No attempt was made to alter the routine activity of the theatre staff.

Both groups underwent a similar pre-anaesthetic sequence; adhesive electrocardiograph electrodes were applied (but not connected to the monitor), a blood pressure cuff was applied and then HR, SAP and RR were noted by the same observer as before. The patient was asked to assess his/her own level of anxiety on the LAAS. Then, anaesthesia was induced.

Each patient was visited after operation and asked to complete the questionnaire shown in Table 6.

Statistical analysis was performed using Student's *t*-test for all comparisons except for the relationship between waiting time in theatre and final LAAS, for which the nonparametric Kendall's Tau test was used.

Results

The two groups were comparable in respect of age, weight, sex, ASA status and the number of previous operations (Table 1). The baseline values of LAAS, HR, SAP and RR measured in the ward on the day before surgery were also similar (Table 2).

There was no significant difference between patients in whom anaesthesia was induced in the anaesthetic room (Group A) and those induced in the theatre (Group B) in respect of anxiety assessed immediately before induction (Table 3).

There was a small increase in anxiety between the baseline values and the pre-induction values when all data were pooled; mean LAAS, HR and SAP increased, although RR decreased. Table 4 shows the changes from baseline to pre-induction values, the differences between Group A and Group B and their significance. The changes in LAAS were analysed to detect any difference between the sexes (Table 5); there was a suggestion that females were more anxious in the anaesthetic room and males more anxious in the theatre.

Table 2. Baseline indices of anxiety on day before operation, expressed as mean (SD).

	Group A (anaesthetic room)	Group B (theatre)
LAAS (mm)	24.7 (16.2)	26.5 (16.2)
Heart rate (beats/minute)	76.1 (10.1)	77.3 (12.6)
Systolic arterial pressure (mmHg)	119.6 (13.4)	120.7 (12.9)
Respiratory rate (per minute)	16.5 (4.1)	16.8 (3.2)

LAAS, linear analogue anxiety score.
No significant differences.

Table 3. Indices of anxiety immediately before induction, expressed as mean (SD).

	Group A (anaesthetic room)	Group B (theatre)
LAAS (mm)	29.7 (19.9)	31.8 (21.8)
Heart rate (beats/minute)	77.4 (12.8)	77.4 (13.4)
Systolic arterial pressure (mmHg)	128.4 (13.4)	132.0 (12.3)
Respiratory rate (per minute)	15.9 (3.5)	15.2 (3.2)

LAAS, linear analogue anxiety score.
No significant differences.

Table 4. Mean changes in the indices of anxiety (baseline to pre-induction) and differences between the two groups.

	Group A (anaesthetic room)	Group B (theatre)	Difference between Group A and Group B
LAAS (mm)	4.9	5.3	0.4 NS
Heart rate (beats/minute)	1.72	0.12	1.6 NS
Systolic arterial pressure (mmHg)	8.8	12.7	3.6 NS
Respiratory rate (per minute)	−0.6	−1.58	0.98*

LAAS, linear analogue anxiety score.
NS, not significant.
*$p<0.05$.

Table 5. Changes in LAAS (baseline to pre-induction) in males and females, expressed as mean with 95% confidence intervals.

	Group A (anaesthetic room)		Group B (theatre)	
	Males ($n=25$)	Females ($n=25$)	Males ($n=25$)	Females ($n=25$)
Mean change in LAAS (mm)	0.5	9.4	7.5	3.0
95% confidence intervals	−6.9, +7.9	+3, +15.8	+2.1, +12.9	−6.2, +12.2

LAAS, linear analogue anxiety score.

Ninety-five percent of patients completed the questionnaire about which aspect of hospital stay worried them most (Table 6). Many patients mentioned other factors for their anxiety; these included anxiety about outcome of surgery, leaving children at home, interruption of breast-feeding, loss of income (self-employed) and postoperative complications. Seventy-three percent of all patients admitted to having some anxiety (64% of males and 76% of females).

An apparent positive correlation between waiting time within the theatre suite and the final LAAS was noticed but this proved not to be statistically significant.

Discussion

Anxiety is subjective and therefore difficult to quantify. Consequently, many subjective and objective methods have been used in its assessment. Subjective methods include scoring systems,[8-10] the Multiple-Affect Adjective Check List (MAACL)[11,12] and the Linear Analogue Anxiety Scale.[13-17] Objective methods include measurement of heart rate, arterial pressure and respiratory rate;[9] conductivity of skin using the galvanic skin response;[18,19] plasma cortisol concentrations;[20] catecholamine excretion;[21] degree of vasoconstriction using digital plethysmography;[22] and plasma catecholamine concentrations.[23] The use of LAAS has become common in the assessment of pain,[24] but has been used widely also in the study of pre-operative anxiety.[13-17] Elliott *et al.* [25] found a strong correlation between MAACL and LAAS and Fell *et al.*[23] found a significant correlation between LAAS and plasma catecholamine concentrations in the assessment of anxiety. LAAS, HR, SAP and RR were selected in this study for their simplicity and noninvasive nature.

Table 6. Results of questionnaire in order of frequency.

Cause for anxiety	Frequency
Thought of pain after operation	26
Fear of not coming round from anaesthesia	23
Waiting for your turn	22
Thought of an operation	19
Fear of being sick after operation	16
Thought of an anaesthetic	12
Coming in to the hospital	10
Fear of being awake during operation	10
Injection and needle	9
Being inside operating theatre	4
Journey to operating theatre	4
Other reasons (see text)	

Our data show that 73% of all patients (64% of males and 76% of females) admitted to anxiety in the peri-operative period, which correlates well with similar previous studies.[26] Most patients in both groups experienced an increase in anxiety in the theatre suite compared to baseline values, as shown by the group mean LAAS, HR and SAP, but RR decreased and did not correlate well with the other indices. None of these changes was statistically significant. The change in Group A (anaesthetic room) was not significantly different from that in Group B (theatre) when expressed as change in anxiety from baseline values. The results from the questionnaire (Table 6) show that of the factors which contribute to patient anxiety, the site of induction did not emerge as a major issue; only four patients (8%) in the theatre group believed that this contributed to their anxiety. It was clear that many factors influence peri-operative anxiety; this confirms the results of other studies.[26-29] Some of the causes are totally unrelated to anaesthesia and surgery but are due to patients' domestic circumstances, such as leaving children at home, loss of income in the self-employed and interruption of breast-feeding. Fear of pain after operation was the commonest cause of anxiety, followed by fear of not waking up, and then waiting in the ward for their summons for operation. Anxiety starts from the day that the patient is told of the need for surgery, and increases gradually during admission, pre-operative investigations and preparation,[27] the journey to theatre and waiting within the theatre suite. It may reach a climax before induction although we have shown that the location of induction is immaterial. Lewis[30] compared anxiety in the anaesthetic room with or without a mural painting and found that there was no significant difference in the level of anxiety between the two groups. We found a positive correlation between the waiting time in the theatre suite before induction and the final LAAS, although this was not statistically significant because of the skewed distribution. Premedication was standardised on the basis of body weight and was thought unlikely to have obscured differences between the groups; however, a further study without premedication may be indicated.

A report on mortality associated with anaesthesia[31] emphasised the importance of an increased level of monitoring of vital signs throughout anaesthesia. The cardiovascular response to laryngoscopy and intubation is well recognised,[32–34] and induction of anaesthesia is a particularly hazardous period;[35] although most of these changes are short-lived and apparently harmless, they have on occasions proved serious or fatal.[36] Unexpected events such as difficult intubation, adverse reactions to drugs, misplaced tracheal tube, laryngospasm, the need for a second dose of suxamethonium with consequent bradycardia, or vomiting and regurgitation may occur at induction and yet the current practice is usually to carry out the induction with the monitoring apparatus in the next room. The unconscious patient is then transferred to theatre with attached infusions, and this rushed transfer is another potential hazard; limbs may be damaged, there may be inadequate support for the head,[37] infusions or catheters may become disconnected, the tracheal tube may be displaced and hypoxia and lightened anaesthesia may result from delayed reconnexion of the breathing system. After this hazardous period, monitoring is started during a relatively quiet period of maintenance anaesthesia when the patient is settled on the table. One expensive option is to have a second set of monitors in the anaesthetic room but there remains a break in continuity during the transfer to theatre. The need to carry out induction of anaesthesia in theatre is generally accepted for Caesarean section, in very ill patients and in small babies. Some day-surgery units, accident units and minor operating theatres do not have an anaesthetic room. Patients who undergo surgery under regional analgesia are exposed to theatre surroundings, apparently without undue anxiety. In many countries, anaesthetic rooms are unknown; anaesthetists who have visited the United States have reported the advantages and disadvantages of induction inside the operating room.[38,39] An editorial in *Anaesthesia*[1] enumerated the advantages of induction in theatre with all the monitoring apparatus *in situ* from the start and suggested that patient acceptance was good. Use of a capnograph at induction would detect a misplaced tracheal tube immediately.[40–42] The saving of time between cases should not take precedence over the increased safety for the patient. The drugs and equipment which at present are stored in the anaesthetic room could be accommodated in a mobile trolley with easy access when needed urgently. The use of wrapped sterile packs of theatre instruments has reduced the frightening arrays of gleaming instruments which used to be a source of anxiety to patients.

The present paper was in an advanced state of preparation when the traditional use of anaesthetic rooms was questioned recently.[43] We have failed to demonstrate that induction of anaesthesia in the operating theatre is a significant source of anxiety to patients, and we suggest that the use of anaesthetic rooms should be reappraised.

Acknowledgments

We thank Mr S. Day, BSc, for help with the design of the study and statistical analysis, Dr D. Zuck for advice and encouragement and Mrs J. Carter and Mrs B. New for secretarial help.

References

1. Editorial. *Anaesthesia* 1974; **29:** 265–8.
2. *Studies in the functions and design of hospitals: The report of an investigation sponsored by the Nuffield Provincial Hospitals Trust and the University of Bristol.* London: Geoffrey Cumberlege, Oxford University Press, 1955.
3. A meeting at the Hospital Centre of the King Edward's Hospital Fund for London on 27 January 1965. Anaesthetic room design. *Anaesthesia* 1965; **20:** 234–5.
4. WHEELER ET, CASSELS WH. Planning the operating room. *Anesthesiology* 1947; **8:** 567–78.
5. OSTLERE G. Aesthetics and anaesthetics; some observations on anaesthetic rooms. *Anaesthesia* 1950; **5:** 91–3.
6. HEWER CL. Anaesthetic rooms. *British Medical Journal* 1955; **2:** 257.
7. STEEL GC. Decoration of the anaesthetic room: a study of patients' reactions. *British Medical Journal* 1959; **1:** 43–5.
8. DUNDEE JW, MOORE J, NICHOLL RM. Studies of drugs given before anaesthesia. I: A method of pre-operative assessment. *British Journal of Anaesthesia* 1962; **34:** 458–63.
9. NISBET HIA, NORRIS W. Objective measurement of sedation. II: A simple scoring system. *British Journal of Anaesthesia* 1963; **35:** 618–23.
10. FORREST WH, BROWN CR, BROWN BW. Subjective responses to six common preoperative medications. *Anesthesiology* 1977; **47:** 241–7.
11. ZUCKERMAN M. The development of an affect adjective check list for the measurement of anxiety. *Journal of Consulting and Clinical Psychology* 1960; **24:** 457–62.
12. WASSENAAR W, LANCEE WJ, GALLOON S, GALE GD. The measurement of anxiety in the pre-surgical patient. *British Journal of Anaesthesia* 1977; **49:** 605–8.
13. MACKAY CJ. In MARTIN I, VENABLES PH, eds. *Techniques in psychophysiology.* Chichester: Wiley, 1980: 501–64.
14. BEECHEY APG, ELTRINGHAM RJ, STUDD C. Temazepam as premedication in day surgery. *Anaesthesia* 1981; **36:** 10–5.
15 BURTON AJ. Recalled apprehension after premedication with lorazepam. *Anaesthesia* 1982; **37:** 1019–21.
16. PINNOCK CA, DERBYSHIRE DR, ELLING AE, SMITH G. Comparison of oral slow release morphine (MST) with intramuscular morphine for premedication. *Anaesthesia* 1985; **40:** 1082–5.
17. FISHER AP, VINE P, WHITLOCK J, HANNA M. Buccal morphine premedication. A double-blind comparison with intramuscular morphine. *Anaesthesia* 1986; **41:** 1104–11.
18. NISBET HIA, NORRIS W, BROWN J. Objective measurement of sedation. IV: The measurement and interpretation of electrical changes in the skin. *British Journal of Anaesthesia* 1967; **39:** 798–804.
19. DONCHIN Y, KATZ A. Emotional reactions during lumbar extradural anaesthesia. *Anaesthesia* 1980; **35:** 822–4.
20. JAMES M, FISHER A. Nitrazepam as a premedicant in minor surgery. An assessment. *Anaesthesia* 1970; **25:** 364–7.
21. MARTINEZ LR, VON EULER C, NORLANDER OP. The sedative effect of premedication as measured by catecholamine excretion. *British Journal of Anaesthesia* 1966; **38:** 780–5.
22. JOHNSTONE M. The effect of lorazepam on the vasoconstriction of fear. *Anaesthesia* 1976; **31:** 868–72.
23. FELL D, DERBYSHIRE DR, MAILE CJD, LARSSON IM, ELLIS R, ACHOLA KJ, SMITH G. Measurement of plasma catecholamine concentrations. An assessment of anxiety. *British Journal of Anaesthesia* 1985; **57:** 770–4.

24. Revill SI, Robinson JO, Rosen M, Hogg MIJ. The reliability of a linear analogue for evaluating pain. *Anaesthesia* 1976; **31:** 1191–8.
25. Elliott P, Pandit SK, Patterson CC, Dundee JW. The plasma concentrations and reduction in anxiety produced by two oral preanaesthetic medications. *British Journal of Anaesthesia* 1984; **56:** 800P.
26. Ramsay MAE. A survey of pre-operative fear. *Anaesthesia* 1972; **27:** 396–402.
27. Thomas E. Pre-and postoperative minor discomforts. *British Journal of Anaesthesia* 1963; **35:** 327–9.
28. Norris W, Baird WLM. Pre-operative anxiety: a study of the incidence and aetiology. *British Journal of Anaesthesia* 1967; **39:** 503–9.
29. Keep PJ, Jenkins JR. From the other end of the needle. The patient's experience of routine anaesthesia. *Anaesthesia* 1978; **33:** 830–2.
30. Lewis R. Pre-operative anxiety and anaesthetic room decor. *Anaesthesia* 1985; **40:** 1024–5.
31. Lunn JN, Mushin WW. *Mortality associated with anaesthesia.* London: Nuffield Provincial Hospitals Trust, 1982.
32. Millar Forbes A, Dally FG. Acute hypertension during induction of anaesthesia and endotracheal intubation in normotensive man. *British Journal of Anaesthesia* 1970; **42:** 618–24.
33. Coleman AJ, Jordan C. Cardiovascular responses to anaesthesia. Influence of beta-adrenoreceptor blockade with metoprolol. *Anaesthesia* 1980; **35:** 972–8.
34. Griffin RM, Phipps JA, Evans IM. Electrocardiographical changes in the peri-operative period. A pilot study. *Anaesthesia* 1985; **40:** 193–7.
35. Prys-Roberts C, Greene LT, Meloche R, Foex P. Studies of anaesthesia in relation to hypertension. II: Haemodynamic consequences of induction and endotracheal intubation. *British Journal of Anaesthesia* 1973; **43:** 531–47.
36. Fox EJ, Sklar GS, Hill CH, Villanueva R, King BD. Complications related to the pressor response to endotracheal intubation. *Anaesthesiology* 1977; **47:** 524–5.
37. Craig J, Wilson ME. A survey of anaesthetic misadventures. *Anaesthesia* 1981; **36:** 933–6.
38. Sykes MK. The American approach to anaesthesia. *British Medical Journal* 1956; **1:** 1148–50.
39. Buxton-Hopkin DA. Some impressions of the teaching and practice of anaesthesia in the United States. *British Journal of Anaesthesia* 1962; **34:** 580–6.
40. Sara CA, Wark HJ. Disconnection: an appraisal. *Anaesthesia and Intensive Care* 1986; **14:** 448–52.
41. Dorsch SE. Endotracheal tube placement. *Anaesthesia and Intensive Care* 1983; **11:** 176.
42. Murray IP, Modell JH. Early detection of endotracheal tube accidents by monitoring carbon dioxide concentration respiratory gas. *Anesthesiology* 1983; **59:** 344–6.
43. Blogg C. E. Sacred cowsheds in anaesthesia. *Anaesthesia News* 1988; **6:** 3.

Anaesthesia, 1989, Volume 44, pages 656–657

CASE REPORT

Laryngeal mask anaesthesia for repair of cleft palate

M. E. BEVERIDGE

Summary

A method of anaesthesia for repair of cleft palate is described. The baby had Pierre Robin syndrome and tracheal intubation had proved to be impossible.

Key words

Equipment; laryngeal mask.
Surgery; cleft palate.

The micrognathia, glossoptosis and cleft palate of the Pierre Robin syndrome constitute a formidable triad among the congenital abnormalities which make for a difficult airway. These babies may present in the early weeks of life with respiratory obstruction, and various manoeuvres have been used to alleviate the symptoms according to their severity. It may be sufficient to nurse the patient in the prone position and thereby allow the tongue to fall forward; occasionally the tongue must be stitched to the lower alveolar margin. Rarely, tracheostomy is required. More room becomes available within the mouth to accommodate the tongue, and the breathing difficulties become less severe with the passage of time and growth of the patient, particularly the mandible. The majority of these patients are not seen by the anaesthetist, however, until surgical repair of the cleft palate is undertaken at about 6 months of age. There may be considerable difficulty in visualising the larynx even at that time, in spite of growth, and there can be few paediatric anaesthetists who have escaped the chagrin of a failed intubation.

Case history

A baby boy who weighed 2.5 kg was noted to have hypoplastic femora and the Pierre Robin syndrome. He presented with a right inguinal hernia at 4.5 months of age, and was admitted to hospital for repair of cleft palate, insertion of grommets and herniotomy. General anaesthesia was induced with thiopentone 25 mg and continued with nitrous oxide, oxygen and halothane supplemented with ether while tracheal intubation was attempted. The vocal cords could not be seen and after three failures it was decided to abandon the cleft palate repair. Grommets were inserted and the herniotomy performed. He was admitted when he was 16 months old for repair of a left inguinal hernia and anaesthesia was successfully achieved using a technique with spontaneous respiration on a facemask. Laryngoscopy was unsuccessful, and not even the epiglottis was seen. He was again presented 3 months later for repair of the cleft palate, but repeated attempts at intubation were unsuccessful and once more the procedure was abandoned.

We paused at this stage to take stock. The paediatric fibreoptic laryngoscope was too big for the appropriate tracheal tube, and we were reluctant to inflict a tracheostomy on a child who already had severe problems. He was still not attempting to speak so there was no immediate urgency about repairing the palate, and we hoped that further growth would make intubation possible.

He was re-admitted at 30 months of age for another attempt at repair of the palate. He weighed 9 kg, but because of leg abnormalities was neither standing nor walking, and although general growth had occurred, he still had a severe degree of micrognathia and had not begun to speak. He had no respiratory problems, and during his previous anaesthetics there had never been any difficulty in maintaining a clear airway. On this occasion, induction with thiopentone 50 mg followed by nitrous oxide, oxygen and halothane allowed a fairly deep level of anaesthesia to be achieved without incident. One brief, unsuccessful attempt at laryngoscopy was made, then a laryngeal mask (Brain size 2)[1,2] was easily placed over the larynx, the cuff inflated and anaesthesia continued with spontaneous ventilation of the same gas and vapour mixture. The tube of the mask emerged through the mouthpiece of the surgeon's gag, and the T-piece connected to it in the usual way. The space round the mask was carefully packed, and the operation proceeded. Access for the surgeon was limited by the tube and the small mouth, but it was possible for the repair

---

M.E. Beveridge, MB, ChB, FFARCS, Consultant Anaesthetist, Honorary Clinical Senior Lecturer, Department of Anaesthesia, Royal Infirmary, Aberdeen AB9 2ZB.

Accepted 19 January 1989.

0003–2409/89/080656+02 $03.00/0 © 1989 The Association of Anaesthetists of Gt Britain and Ireland

to be completed satisfactorily. The pack was removed at the end, and the patient breathed oxygen and air until he was beginning to swallow, when the cuff was deflated and the mask gently removed. Severe respiratory obstruction occurred at this moment, and the tongue had to be pulled well forward by traction on the tongue stitch before the airway was cleared. A nasopharyngeal tube was left in place for 24 hours but once it was removed there was no further problem.

There was a certain amount of blood on the upper surface of the mask when it was removed in spite of the pharyngeal pack, and, more significantly, there was a small formed blood clot on the underside of the mask. The child coughed up a mixture of mucus and blood for a few hours after operation but a chest X ray showed that the lung fields were clear. His subsequent progress has been uneventful.

Discussion

It is important for babies with a cleft palate deformity to have the repair carried out before they have begun to speak. The habit of nasal escape once learned may be difficult to eradicate, even if anatomical closure of palate and pharyngeal wall has been achieved by surgery. It was not possible in this patient to provide safe operating conditions without the use of the laryngeal mask. Fortunately, because of his developmental delay our patient had not yet started to speak and we are hopeful that when he does any problem will not be due to his cleft palate. The method described here is not to be recommended as that of choice, but when tracheal intubation is impossible it is an effective way to allow surgery to proceed without the necessity for a tracheostomy. Once tracheostomy is instituted, decannulation can be extremely difficult, and indeed it is not without its own inherent hazards. The instructions which accompany the laryngeal mask stress that it be not used on patients at risk of regurgitation of stomach contents. The presence of blood clot on the underside of the mask on this occasion confirms the wisdom of this advice, since clearly it is possible for material in the pharynx to bypass the cuff of the mask and enter the trachea. However, if at any time there had been a significant accumulation of blood and mucus in the pharynx, we would have detected it by auscultation, and the surgeon could have sucked it out there and then. What we achieved was safe delivery of the anaesthetic gas mixture directly to the larynx, and reasonable surgical access without interference with the airway.

Acknowledgments

My thanks are due to Dr A.I.J. Brain of Brain Medical Ltd for the loan of the mask used in this case. Without his generosity the operation would have been much more complicated. I am also grateful to Mr O. Fenton, Consultant in Plastic Surgery, for his patience and forbearance.

References

1. Brain AIJ. The laryngeal mask—a new concept in airway management. *British Journal of Anaesthesia* 1983; **55**: 801–5.
2. Brain AIJ, McGhee TD, McAteer EJ, Thomas A, Abu-Saad MAW, Bushman JA. *Anaesthesia* 1985; **40**: 356–61.

Anaesthesia, 1989, Volume 44, pages 658–659

CASE REPORT

Asystole with convulsion following a subanaesthetic dose of propofol plus fentanyl

K. L. DORRINGTON

Summary

A case is presented in which asystole and convulsions occurred after an attempted induction of anaesthesia with propofol and fentanyl. The case suggests that a history of syncope may be associated with unusual susceptibility to the bradycardic effects of propofol.

Key words

Anaesthetics, intravenous; propofol.
Complications; asystole, convulsion.

This is a report of a life-threatening reaction to the attempted induction of anaesthesia in an apparently healthy young man. The case illustrates the value of eliciting a history of syncope, and the usefulness of routine electrocardiographic (ECG) monitoring at induction of anaesthesia.

Case history

A 22-year-old male who weighed 75 kg was scheduled as a day case for reduction of a fractured nose under general anaesthesia. The injury was sustained 2 weeks earlier during a rugby match. The patient had never previously been anaesthetised, denied drug therapy or allergy, and admitted to no serious ill health. Premedication was not given.

The patient looked relaxed on arrival in the anaesthetic room. A brief explanation was provided of the proposed monitoring, insertion of a cannula, pre-oxygenation, and induction. An ECG monitor was connected via chest electrodes. Venous access was obtained by insertion of a 20-gauge cannula into a left antecubital vein, with distracting thumb pressure to the forearm and no local anaesthetic. The patient claimed not to have felt the needle. Arterial blood pressure was 130 mmHg systolic and the ECG showed sinus rhythm at 85 beats/minute. Pre-oxygenation was begun by asking the patient to hold in place a facemask connected to a Bain system that received oxygen at 10 litres/minute.

Fentanyl 50 μg was injected through the cannula, followed by 0.5 ml 2% lignocaine to prevent pain on the administration of propofol. Injection of the propofol was started after approximately 90 seconds, but was stopped after 7 ml when rapid dilatation of the pupils and extreme pallor were noticed. The ECG trace showed no activity. Cardiac arrest was diagnosed and further assistance called.

Manual ventilation by mask with oxygen was easily performed. Fifteen seconds into asystole tonic–clonic movements of the whole body began. The convulsion subsided about 45 seconds into asystole and complexes spontaneously appeared on the ECG at a slow rate. Atropine 0.6 mg was administered intravenously, and resulted after a further 30 seconds in a junctional rhythm at a rate of 70 beats/minute and a systolic arterial blood pressure of 155 mmHg. The patient rapidly became conscious. There was no incontinence or post ictal drowsiness. Surgery was postponed. A 12-lead ECG at one hour after the event showed mild ST elevation over the chest leads which persisted until discharge 48 hours later. Cardiac enzymes at 6 hours were normal.

The patient admitted two previous episodes of collapse when questioned later; both had occurred in hospital. He collapsed on the first occasion at age 17 years and convulsed during the aspiration of fluid from a knee. He again collapsed at age 18 years during venepuncture for blood sampling in a genito-urinary clinic. No convulsion was reported.

Medical review prior to discharge revealed mild postural hypotension and no other abnormality.

K.L. Dorrington, DPhil, DA, Nuffield Research Fellow, Nuffield Department of Anaesthetics, John Radcliffe Hospital, Oxford OX3 9DU.

Accepted 15 February 1989.

0003–2409/89/080658+02/$03.00/0

© 1989 The Association of Anaesthetists of Gt Britain and Ireland

Discussion

Propofol is an agent which is increasingly used in day case surgery. Its tendency to induce bradycardia may result from a direct action on the atrial sinus,[2] as well as by resetting the baroreflex.[3]

Awareness of this tendency is advised when induction of anaesthesia is supplemented by vagotonic drugs such as fentanyl and suxamethonium.[4] A history of syncopal arrest was elicited in a case of persistent bradycardia after propofol,[5] similar to this patient.

This is the first report of asystole that led to a generalised convulsion after attempted induction with propofol. The dose involved (1 mg/kg) is less than half the usual induction dose (2–3 mg/kg).[1] The convulsion is presumed in this case to have been a consequence of asystole,[6] though both propofol[7] and fentanyl[8] may have modified its duration. ECG monitoring helped to distinguish asystole from a primary seizure, as in a previous case with a similar time-scale in which asystole resulted from fear alone.[9]

Patients who are prone to syncope may be unusually susceptible to the bradycardic effects of propofol.

References

1. Sanderson JH, Blades JF. Multicentre study of propofol in day case surgery. *Anaesthesia* 1988; **43** (Suppl.): 70–3.
2. Colson P, Barlet H, Roquefeuill B, Eledjam J-J. Mechanism of propofol bradycardia. *Anesthesia and Analgesia* 1988; **67**: 906–7.
3. Cullen PM, Turtle M, Prys-Roberts C, Way WL, Dye J. Effect of propofol anesthesia on baroreflex activity in humans. *Anesthesia and Analgesia* 1987; **66**: 1115–20.
4. Baraka A. Severe bradycardia following propofol–suxamethonium sequence. *British Journal of Anaesthesia* 1988; **61**: 482–3.
5. Thomson SJ, Yate PM. Bradycardia after propofol infusion. *Anaesthesia* 1987; **42**: 430.
6. Ziegler DK, Lin J, Bayer WL. Convulsive syncope: relationship to cerebral ischemia. *Transactions of the American Neurological Association* 1978; **103**: 150–4.
7. Simpson KH, Halsall PJ, Carr CME, Stewart KG. Propofol reduces seizure duration in patients having anaesthesia for electroconvulsive therapy. *British Journal of Anaesthesia* 1988; **61**: 343–4.
8. Rosenberg M, Lisman SR. Major seizure after fentanyl administration: two case reports. *Journal of Oral and Maxillofacial Surgery* 1986; **44**: 577–9.
9. Schraeder PL, Pontzer R, Engel TR. A case of being scared to death. *Archives of Internal Medicine* 1983; **143**: 1793–4.

Anaesthesia, 1989, Volume 44, pages 660–662

CASE REPORT

Heat stroke—an uncommon presentation

P. V. VAN HEERDEN AND C. H. COLLINS

Summary

A case of heat stroke is reported in which there was a delayed diagnosis and a fatal outcome. Recent literature is reviewed.

Key words

Heat stroke.

Heat stroke is the most severe form of a range of syndromes associated with exposure to high environmental temperature. The other syndromes are heat cramps, heat exhaustion and exertional heat injury.[1] Mortality is approximately 30% and although fatal heat stroke is reported regularly from countries with warmer climates, it is seen rarely in Britain.[2]

We report the case of a patient who was admitted to our Intensive Care Unit (ICU) and in whom there was a delayed diagnosis and a fatal outcome.

Case history

The patient, a 63-year-old Caucasian male, was referred to an outlying hospital late in the evening with a history of epileptiform seizures which had started suddenly whilst haymaking. The patient had spent all day haymaking in the July sun. The only other history available was that the patient was known to have a bipolar affective disorder, for which he was being treated with procyclidine, amitriptyline, and flupenthixol.

Treatment at the outlying hospital consisted of intravenous diazepam, which did not control the fits. He was referred to our hospital for control of the status epilepticus and further investigation because of failure to respond to what was considered adequate treatment.

The patient arrived in the Accident and Emergency Department of our hospital at approximately midnight, 2 hours after the initial onset of epileptiform seizures. Examination revealed an unkempt male patient, unconscious, with a Glasgow coma score of 3; convulsions were still present. He was shocked, with a blood pressure of 80/50 mmHg and a pulse rate of 140 beats/minute. Examination of the chest revealed widespread inspiratory crepitations and there was some concern that he had aspirated gastric contents into his tracheobronchial tree. This suspicion was supported by a chest radiograph which showed right-sided shadowing consistent with aspiration. Examination of the abdomen was unremarkable. His temperature recorded at the time of admission was 42°C measured in the axilla. His extremities were cool to the touch.

The pyrexia and central nervous system symptoms were consistent with a diagnosis of meningitis, and the cerebrospinal fluid was examined; it was normal. The results of other investigations are shown in Table 1. In addition, blood was taken for bacteriological culture.

The electrocardiogram was normal except for a sinus tachycardia. Treatment in the Accident and Emergency Department included intravenous infusion of fluids (0.9% saline and polygeline) and the institution of antibiotic therapy with cefuroxime and metronidazole. He received further intravenous diazepam which controlled the seizures. Oxygen was administered by Ventimask.

He remained seriously ill and deeply unconscious at 0300

Table 1. Results of investigations.

Haemoglobin concentration	15 g/dlitre
White cell count	14.1×10^9/litre
Platelet count	312×10^9/litre
Serum sodium	140 mmol/litre
Serum potassium	6.3 mmol/litre (reported as '?haemolysed sample')
Random serum glucose	5.1 mmol/litre
Arterial blood gas (on room air)	pH 7.34 $P\text{CO}_2$ 3.5 kPa $P\text{O}_2$ 5.4 kPa Base excess −7.3 mmol/litre Standard bicarbonate 18.4 mmol/litre
Urine dipstick test	Protein + + + + Blood + + + +

P.V. van Heerden, MB, BCh, DA (SA), FFARCSI, Registrar, C.H. Collins, MB, BS, FFARCS, Consultant, Anaesthetic Department, Royal Devon and Exeter Hospital, Barrack Road, Exeter EX2 5DW.

Accepted 20 February 1989.

0003–2409/89/080660+03 $03.00/0
© 1989 The Association of Anaesthetists of Gt Britain and Ireland

hours and was referred to ICU for control of his airway, control of the seizures and supportive therapy. The patient convulsed again on arrival in the ICU and it was decided to control the seizures with intravenous thiopentone and to intubate the trachea to prevent further tracheobronchial soiling. Intermittent positive pressure ventilation (IPPV) was instituted and arterial blood gas measurements revealed a requirement for an inspired oxygen concentration of 70% and a minute volume of 12 litres/minute.

A central venous line was inserted and further fluid therapy was given, guided by central venous pressure (CVP) measurements. Benzylpenicillin was added to the existing antibiotic regimen. The presumptive differential diagnoses at this stage, made by the admitting registrar, included heat stroke and the neuroleptic malignant syndrome.

His condition followed a rapidly downhill course, despite the initial treatment, with progressive failure of various organ systems over the next 15 hours. He remained hypotensive despite adequate cardiac filling pressures (as estimated by a flow-directed pulmonary artery catheter) and the introduction of inotropic doses of dopamine. His rectal temperature decreased from 40.3°C on admission to ICU to 38.5°C after surface cooling by means of electric fans. His peripheral (toe) temperature ranged from 20 to 29°C and there was marked peripheral cyanosis.

Further complications included worsening hypoxaemia, (an inspired oxygen concentration of 100% and positive end-expiratory pressure were required) and radiographic features of the adult respiratory distress syndrome. Renal function deteriorated with a progressive increase in serum urea and creatinine concentrations, associated with oliguria. A consumptive coagulopathy developed which resulted in a generalised petechial rash and fresh blood in the nasogastric aspirate. Hypoglycaemia developed also, and was treated with intravenous glucose.

The patient developed abdominal distension and bloody diarrhoea, with the disappearance of bowel sounds. These signs, together with a slight increase in serum amylase concentration, were consistent with several possible causes, e.g. acute pancreatitis, florid gastroenteritis or ischaemic colitis. These diagnoses were entertained despite the initial differential diagnoses of the ICU registrar.

The patient's condition continued to deteriorate and he developed intractable multisystem organ failure despite maximum intensive care support. He died 15 hours after admission to ICU.

Discussion

The diagnosis of heat stroke was included in the ICU registrar's initial differential diagnoses, but was not followed up, even though in retrospect this patient presented with features of hyperthermia, altered cerebral function and hypohydrosis, the classical triad of heat stroke.[3] He had also been exposed to a number of the predisposing risk factors for heat stroke, namely, the use of anticholinergic drugs (procyclidine), age (more common in the elderly),[1] exposure to high ambient temperature and humidity[4] and unaccustomed exercise in heavy clothing. Other risk factors for heat stroke include pre-existing chronic disease (arteriosclerosis and congestive heart failure), diuretic therapy, diabetes mellitus, alcoholism, skin disorders which restrict heat loss (e.g. scleroderma), military basic training and long distance running.[1]

Exposure to high environmental temperatures, in association with the risk factors above, produces a range of clinical syndromes. These are heat cramps, heat exhaustion, exertional heat injury, and heat stroke.[1] The clinical features of these syndromes overlap and the severity of signs and symptoms is related to the number of risk factors present and the duration and degree of exposure to high environmental temperatures. Patients with heat stroke present classically with altered cerebral function (which may include lethargy, stupor, delirium or coma), hot dry skin (hypohydrosis, with or without piloerection) and increased core temperature. They may complain of dizziness, nausea or headache. Signs of hypovolaemic shock and hyperventilation are usually present. The patient may be areflexic and flaccid.[1]

The florid secondary complications, as displayed by our patient, develop if no action is taken at this early stage. These include a consumptive coagulopathy, acute renal failure and convulsions. Patients who survive the initial episode may develop delayed secondary complications such as myocardial infarction, heart failure, liver failure, septicaemia and bronchopneumonia; these may occur a few days or a few weeks after the initial presentation.[1]

Special investigations performed on patients with heat stroke may reveal haemoconcentration, leucocytosis, elevated serum urea and creatinine concentrations, hypocalcaemia, hypokalaemia, hypophosphataemia, respiratory alkalosis and metabolic acidosis. Electrocardiographic changes may be present and include sinus tachycardia, ST segment depression, T wave flattening, and evidence of myocardial infarction. There may also be laboratory evidence of hepatocellular dysfunction, consumptive coagulopathy and thrombocytopenia. Urinalysis abnormalities may include proteinuria and haematuria.[1]

This patient's history of medication with flupenthixol resulted in a possible differential diagnosis of neuroleptic malignant syndrome (NMS). NMS is a rare complication of neuroleptic drug therapy[5] and is characterised by hyperthermia, muscular rigidity, altered consciousness and autonomic instability.[6] NMS may present atypically with clinical features suggestive of heat stroke and adult respiratory distress syndrome,[7] which would be more in keeping with our patient's presentation.

The third possibility, although unlikely in this setting, is an episode of malignant hyperthermia (MH) triggered by stress. Recent case reports in a patient with a head injury[8] and a young athlete[9] have suggested that stress can trigger MH.

Heat stroke, NMS and MH, are the major disorders associated with high body temperature.[1] The symptoms are well defined, but the pathogenesis is less clear, except in MH. There is said to be a lack of thermoregulatory control in heat stroke,[10] so that heat production is greater than heat loss; the onset of heat stroke is related to the accumulated time at or near the critical thermal maximum temperature of 42°C.[3] Our patient presented to the outlying hospital at 2200 hours, after a full day in the sun, and arrived 2 hours later at our hospital with a temperature of 42°C; it is not surprising that the syndrome was so florid in its presentation. He was still fully dressed in heavy clothing when he presented to our hospital.

Many of the secondary features of heat stroke, such as prerenal renal failure and consumptive coagulopathy, are similar to those that occur in systemic endotoxaemia. Recent experimental work[11-14] supports this view and suggests that cardiovascular adaptation to the combination of increased core temperature and exercise causes excessive shifts of blood flow away from the splanchnic bed to the exercising muscle and limb skin.[3,15] This diversion of blood from the splanchnic bed may result in leakage of lipopolysaccharide endotoxins from the gastrointestinal tract into the circulation[11] and so produce a systemic endotoxaemia.

NMS is similar to MH in that the features of hyperthermia, muscular rigidity and myoglobinuria[16] may occur in either condition. However, there is evidence to show that there is no common pathophysiological link between NMS and MH,[17] although this remains controversial. The pathogenesis of NMS is unclear; it may be related to central dopamine antagonism or to the increased heat production caused by extreme muscle spasm.[18]

The treatment of heat stroke 'requires heroic emergency measures'[1] and includes immediate thermal resuscitation by means of surface cooling;[3] this is said to be more effective than iced gastric lavage.[19] Surface cooling may be performed by simple means such as spraying tap water over the patient and application of an electric fan,[19] to such inventive and expensive methods as the downdraught from a helicopter.[20]

Rapid cooling to a core temperature of 38.5–39°C is advocated, followed by closely monitored passive cooling.[3] Fluid therapy with isotonic saline or half-strength saline with 5% dextrose is started simultaneously; excessive fluid administration should be avoided to prevent the development of cerebral oedema.[3] Subsequent fluid therapy should be guided by serum electrolyte and glucose measurements. The patient is observed for the development of secondary complications after therapy has been instigated. Monitoring of CVP and urine output, and control of the airway, may be required depending on the condition of the patient at the time of presentation.[1] Complications and mortality are related to the delay in achievement of a body temperature less than 40°C.[3]

Recent advances in the treatment of heat stroke include the use of specially designed and effective cooling methods, such as the King Saud University cooling bed,[21] the use of dantrolene[22] and the experimental use in animals of anti-lipopolysaccharide antibodies, steroids and oral antibiotics[12-14] to counter the effects of absorbed endotoxins.

The basic treatment of heat stroke relies heavily on rapid surface cooling and adequate intravenous fluid replacement despite these new and experimental modes of therapy. This treatment is simple and effective if introduced early in the course of the disease.[3] More recent methods of treatment may prove to be more effective in patients, such as ours, in whom initial treatment was delayed and in whom secondary complications have already set in.

The diagnosis in our patient was made too late, although it was obvious retrospectively. Aggressive surface cooling was not instituted and the disease followed a fatal course.

References

1. Petersdorf RG, Root RK. Disturbance of heat regulation. In: Braunwald E, Isselbacher KJ, Petersdorf RG, Wilson JD, Martin JB, Fauci AS, eds. *Harrison's principles of internal medicine*. New York: McGraw Hill, 1987: 42–7.
2. Whitworth JAG, Wolfman MJ. Fatal heat stroke in a long distance runner. *British Medical Journal* 1983; **287:** 948.
3. Hanson PG, Zimmerman SW. Exertional heatstroke in novice runners. *Journal of the American Medical Association* 1979; **242:** 154–7.
4. Zelenak RR, Miller K. Morning report at Charity Hospital: heat stroke New Orleans style. *American Journal of the Medical Sciences* 1987; **294:** 268–74.
5. Gelenberg AJ, Bellinghausen B, Wojcik JD, Falk WE, Sachs GS. A prospective survey of neuroleptic malignant syndrome in a short-term psychiatric hospital. *American Journal of Psychiatry* 1988; **145:** 517–8.
6. Parikh AM, Camara EG. Neuroleptic malignant syndrome. *American Family Physician* 1988; **37:** 296–8.
7. Johnson MD, Newman JH, Baxter JW. Neuroleptic malignant syndrome presenting as adult respiratory distress syndrome and disseminated intravascular coagulation. *Southern Medical Journal* 1988; **81:** 543–5.
8. Feuerman T, Gade GF, Reynolds R. Stress-induced malignant hyperthermia in a head-injured patient. Case report. *Journal of Neurosurgery* 1988; **68:** 297–9.
9. Pamukcoglu T. Sudden death due to malignant hyperthermia. *American Journal of Forensic Medicine and Pathology* 1988; **9:** 161–2.
10. Danzl DF. Hyperthermic syndromes. *American Family Physician* 1988; **37:** 157–62.
11. Gathiram P, Gaffin SL, Brock-Utne JG, Wells MT. Time course of endotoxemia and cardiovascular changes in heat-stressed primates. *Aviation, Space and Environmental Medicine* 1987; **58:** 1071–4.
12. Gathiram P, Wells MT, Brock-Utne JG, Gaffin SL. Prevention of endotoxaemia by non-absorbable antibiotics in heat stress. *Journal of Clinical Pathology* 1987; **40:** 1364–8.
13. Gathiram P, Wells MT, Brock-Utne JG, Wessels BC, Gaffin SL. Antilipopolysaccharide improves survival in primates subjected to heat stroke. *Circulatory Shock* 1987; **23:** 157–64.
14. Gathiram P, Gaffin SL, Brock-Utne JG, Wells MT. Prophylactic corticosteroid suppresses endotoxemia in heat-stressed primates. *Aviation, Space and Environmental Medicine* 1988; **59:** 142–5.
15. Hales JR, Khogali M, Fawcett AA, Mustafa MK. Circulatory changes associated with heat stroke: observations in an experimental animal model. *Clinical and Experimental Pharmacology and Physiology* 1987; **14:** 761–77.
16. Araki M, Takagi A, Higuchi I, Sugita H. Neuroleptic malignant syndrome: caffeine contracture of single muscle fibers and muscle pathology. *Neurology* 1988; **38:** 297–301.
17. Krivosic-Horber R, Adnet P, Guevart E, Theunynck D, Lestavel P. Neuroleptic malignant syndrome and malignant hyperthermia. *In vitro* comparison with halothane and caffeine contracture tests. *British Journal of Anaesthesia* 1987; **59:** 1554–6.
18. Sullivan CF. A possible variant of the neuroleptic malignant syndrome. *British Journal of Psychiatry* 1987; **151:** 689–90.
19. White JD, Riccobene E, Nucci R, Johnson C, Butterfield AB, Kamath R. Evaporation versus iced gastric lavage treatment of heat stroke: comparative efficacy in a canine model. *Critical Care Medicine* 1987; **15:** 748–50.
20. Poulton TJ, Walker RA. Helicopter cooling of heatstroke victims. *Aviation, Space and Environmental Medicine* 1987; **58:** 358–61.
21. Al-Aska AK, Abu-Aisha H, Yaqub B, Al-Harthi SS, Sallam A. Simplified cooling bed for heatstroke. *Lancet* 1987; **1:** 381.
22. Lydiatt JS, Hill GE. Treatment of heat stroke with dantrolene. *Journal of the American Medical Association* 1981; **246:** 41–2.

Anaesthesia, 1989, Volume 44, pages 663–664

CASE REPORT

Pneumothorax caused by minitracheotomy

J. M. SILK AND A. M. MARSH

Summary

We describe a case in which misplacement of a minitracheotomy tube produced a pneumothorax, a complication which has not been reported previously. Methods to identify correct placement of the minitracheotomy tube are discussed.

Key words

Equipment; minitracheotomy.
Complications; pneumothorax.

Minitracheotomy has become accepted as a useful technique to provide an emergency airway or for tracheal toilet in patients with sputum retention, although the procedure is not without risk.[1-3] Haemorrhage,[4] misplacement[5,6] and surgical emphysema[7] are all described. In our case, a misplaced minitracheotomy tube was associated with a pneumothorax.

Case history

A 48-year-old woman with no history of respiratory disease was admitted to the intensive care unit after a craniotomy for clipping of a posterior inferior cerebellar artery aneurysm. Initially she made a good recovery; the only neurological deficit was a mild right-sided weakness. She deteriorated later and insertion of a ventricular drain was carried out.

Four days after the second operation, she became tachypnoeic with a respiratory rate of 40 per minute, and copious secretions were reported by the physiotherapists. Aspiration of the secretions became increasingly difficult and arterial blood gases showed progressive hypoxaemia, despite an increased inspired oxygen concentration. She retained her gag reflex although her neurological condition was poor. Consequently, a minitracheotomy was performed percutaneously under local anaesthesia in the manner recommended by the manufacturers (Portex). The surgeon was satisfied that the distal end of the minitracheotomy tube was in the trachea because warm air was felt coming out through the tube during expiration, and a suction catheter was passed easily.

Her worsening hydrocephalus necessitated the urgent insertion of a ventriculo-peritoneal shunt. This was performed before a chest X ray could be taken to check the position of the minitracheotomy tube. The shunt was inserted under general anaesthesia. The trachea was intubated and the lungs ventilated mechanically; the minitracheotomy was left *in situ*. No problems were encountered during this procedure, and the trachea was extubated and the patient returned to the intensive care unit when the operation had finished. A postoperative chest X ray revealed a large left-sided pneumothorax; the minitracheotomy tube was clearly extratracheal (Fig. 1). The minitracheotomy tube was removed. An intercostal tube was inserted and connected to an underwater seal drain. The left lung had re-expanded completely by the following day. A new minitracheotomy tube was inserted successfully under local anaesthesia, and was still in place at the time of her discharge to another hospital 6 weeks later.

Discussion

The technique of cricothyroidotomy has gained in popularity since the reservations of Chevalier Jackson were dispelled by Brantigan and Grow in 1976.[8] The use of minitracheotomy was described first in 1984 for the treatment of sputum retention[1] and its use is now widespread in intensive therapy units.

The incidence of complications associated with tracheostomy may be as high as 49.3%[9] and pneumothorax is a recognised complication.[10] By contrast, the complication rate associated with cricothyroidotomy is only 6.1%.[8] A

J.M. Silk, MB, BS, FFARCS, A.M. Marsh, MB, BS, MRCP, FFARCS, Senior Registrars, Department of Anaesthesia, The National Hospital for Nervous Diseases, Queen Square, London WC1N 3BG.

Accepted 31 January 1989.

0003–2409/89/080663+02 $03.00/0

© 1989 The Association of Anaesthetists of Gt Britain and Ireland

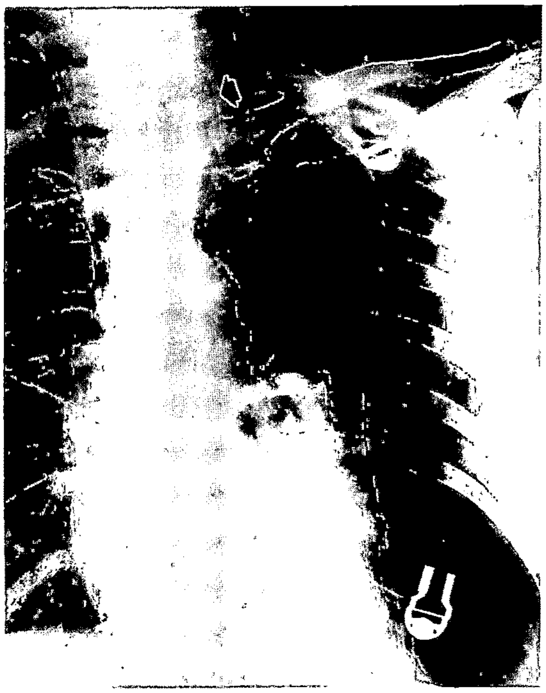


Fig. 1. Chest X ray showing a left-sided pneumothorax. The minitracheotomy tube is arrowed.

number of complications of minitracheotomy have been reported,[4,11] although their incidence is not known. It seems reasonable to expect fewer complications with the smaller operation of minitracheotomy, but misplacement may be more common than in the larger procedure because the insertion of the tube is blind. In the present case, misplacement of the minitracheotomy tube was not recognised immediately and was associated with a pneumothorax.

Misplacement of orotracheal or nasotracheal tubes is not uncommon, can be difficult to recognise, and may be a disaster for the patient.[12] However, the established methods for detecting incorrect positioning of a tracheal tube[13,14] may be deceptive in confirming correct placement of a minitracheotomy tube. A high index of suspicion is one of the most useful safeguards against inadvertent misplacement.

The intrapleural position of the tip of the minitracheotomy tube in the present case resulted in free flow of air with ventilation because the tube was subjected to cyclical changes in intrathoracic pressure. Auscultation over the orifice of the tube would also have been misleading.

Coughing on insertion of a suction catheter and aspiration of secretions usually confirm correct placement. However, in this case the nursing staff reported aspiration of secretions, although these must have resulted from an increased pleural exudate caused by the presence of a foreign body.

The diagnosis of misplacement was made on the chest X ray findings. This investigation is essential after insertion of a minitracheotomy tube, both to confirm correct placement and to exclude complications.

Identification of tracheal rings with a fibreoptic laryngoscope has been suggested as a method of confirming placement of tracheal tubes.[15] This is an attractive concept, but the instruments available currently will not pass through the 4-mm internal diameter of a minitracheotomy tube.

The method of air injection followed by aspiration, described by Wee,[16] might be successful in determining the position of a minitracheotomy tube, although it may be unwise to risk the injection of any volume of air into the paratracheal tissues. In any event, the test might fail in the presence of a pneumothorax, as the injected air could be reaspirated.

Identification of physiologically significant quantities of carbon dioxide in the expired gas must represent the most certain method of confirming rapidly the correct placement of both tracheal[17] and minitracheotomy tubes. Capnography is available widely, and we suggest that its use be employed routinely whenever possible. However a check chest X ray, both anteroposterior and lateral, is still mandatory because capnography may fail to detect the upwards migration of a minitracheotomy tube through the larynx, which is another complication reported recently.[18] The possibility of a pneumothorax should be borne in mind and excluded if misplacement is thought to have occurred.

Acknowledgments

The authors thank Dr I. Calder and Mr M. Powell for their help in preparing the manuscript.

References

1. Matthews HR, Hopkinson RB. Treatment of sputum retention by minitracheotomy. *British Journal of Surgery* 1984; **71:** 147–50.
2. Lewis GA, Hopkinson RB, Matthews HR. Minitracheotomy. A report of its use in intensive therapy. *Anaesthesia* 1986; **41:** 931–5.
3. Layman PR. Cricothyrotomy devices. *Today's Anaesthetist* 1988; **3:** 125–29.
4. Gwynn BR, Mostafa SM. Complications of a minitracheotomy. *Journal of the Royal College of Surgeons of Edinburgh* 1984; **29:** 381.
5. Charnley RM, Verma R. Inhalation of a minitracheotomy tube. *Intensive Care Medicine* 1986; **12:** 108–9.
6. Ravalia A, Stockwell MA. Displacement of a minitracheotomy tube during high frequency jet ventilation. *Anaesthesia* 1987; **42:** 1306–7.
7. Wagstaff A, Sparling R, Ryan DW. Minitracheostomy. *Anaesthesia* 1987; **42:** 216.
8. Brantigan CO, Grow JB. Cricothyroidotomy: elective use in respiratory problems requiring tracheotomy. *Journal of Thoracic and Cardiovascular Surgery* 1976; **71:** 72–80.
9. McClelland RMA. Complications of tracheostomy. *British Medical Journal* 1965; **2:** 567–9.
10. Stauffer JL, Olson DE, Petty TL. Complications and consequences of endotracheal intubation and tracheotomy. A prospective study of 150 critically ill adult patients. *American Journal of Medicine* 1981; **70:** 65–76.
11. Clifton P, Mostafa SM. Complications of minitracheotomy. *Today's Anaesthetist* 1987; **2:** 189–90.
12. Scott DB. Endotracheal intubation: friend or foe? *British Medical Journal* 1986; **292:** 157–8.
13. Kerr JH. Is the tube in the trachea? *British Medical Journal* 1987; **295:** 400.
14. Howells TH, Reithmuller RJ. Signs of endotracheal intubation. *Anaesthesia* 1980; **35:** 984–6.
15. Coe PA, Towey RM. Is the tube in the trachea? *British Medical Journal* 1987; **295:** 723.
16. Wee MYK. The oesophageal detector device. Assessment of a new method to distinguish oesophageal from tracheal intubation. *Anaesthesia* 1988; **43:** 27–9.
17. Birmingham PK, Cheney FW, Ward RJ. Esophageal intubation: a review of detection techniques. *Anesthesia and Analgesia* 1986; **65:** 886–91.
18. West KJ, Coad NR. An unusual complication of minitracheostomy. *Today's Anaesthetist* 1988; **3:** 241.

Anaesthesia, 1989, Volume 44, pages 665–669

APPARATUS

A computer-controlled anaesthetic gas mixer

R. W. BOADEN, P. HUTTON AND C. MONK

Summary

The theory and construction of a prototype computer-controlled gas mixer and flow regulator are described. The device is capable of controlling and mixing flows of oxygen, nitrous oxide and air. The accuracy and repeatability of the device is very high under given conditions, and its performance is quantified. The flow rate and oxygen concentration are selected from a microcomputer and the control program is written in BASIC. Possible improvements to the system are discussed as are uses in both clinical and research work.

Key words

Equipment; flowmeters, gas mixer, computer.
Computers; control.

The advent of low cost microcomputers provides the anaesthetist with the opportunity to use them in many applications. Should it prove possible to control both the composition and flow rate of anaesthetic gases reliably by means of a microcomputer, then the accuracy and flexibility of control may be useful for both clinical and experimental purposes. This paper describes the design and development of such a device linked to a low cost microcomputer. It is an extension of previously reported work on a Digital Flow Regulator.[1]

The possibility of adapting existing manual systems to accomplish computer control of gas mixing and flow regulation was examined first. The two methods in use are firstly a high pressure gas blender followed by a needle valve, or secondly two independent needle valves, one for each gas. Both methods require rotary action. This is perfectly feasible with a microcomputer using a servo or stepping motor but requires positional feedback for accuracy. An improvement on this is to use feedback signals from the gas mixture itself. This requires devices such as an oxygen electrode together with a flow transducer. Both have to be accurate and reliable, which are features often difficult to find.

An approach often taken in industrial situations is to use a self-contained mass flow controller for each gas with the mixture selected by microcomputer. A mass flow controller consists of a mass flow detector that provides a feedback signal to a proportioning solenoid valve. These devices are accurate but very expensive. In the device described in this paper a digital flow regulator is used for each gas and a microcomputer apportions the flows to obtain the desired gas mixture and flow rate.

A digital flow regulator was first described by Langill *et al.* in 1969 though in a different form.[2] The present equipment uses an eight-bit microcomputer and the signal output is in the form of eight digital lines with each line connected to a solenoid valve. These valves supply high pressure gas to their own precalibrated needle valves. The bank of eight needle valves is individually preset in a binary sequence; each flow doubles the previous one. This provides a flow range of 255 to one. Thus with a minimum gas flow of 50 ml/minute, the maximum for a single gas controller would be 12 750 ml/minute, providing any flow in between in steps of 50 ml/minute. Needle valves, when used under these conditions, have been shown to function as sonic nozzles,[3] devices in which mass flow rate varies little in response to downstream pressure changes.

A similar method was used by Cooper *et al.*[4] in a design for a new anaesthetic machine. This machine incorporates a custom-built eight-element digital flow controller for each gas. The microprocessor in the machine directly mixes gases and regulates flow. Another approach to digital control of gas mixing was described by Lundsgaard *et al.* in 1977.[5] The device was manually operated but the flow rate through each equivalent digital line was preset by means of calibrated lengths of fine-bore tubing.

A detailed description of a digital flow regulator may be found in an earlier paper.[1] The impetus to develop stand-alone devices such as this is an attempt to provide low cost components for feedback control of physiological systems

---

R.W. Boaden,* BSc, MB, BS, FFARCS, Senior Registrar, P. Hutton,† BSc, MB, BS, PhD, FFARCS, Lecturer, C. Monk, MB, BS, FFARCS, Senior Registrar, Sir Humphry Davy Department of Anaesthetics, Bristol Royal Infirmary, Bristol.
Also at: *Royal Devon and Exeter Hospital, Exeter,† Queen Elizabeth Hospital, Birmingham.

Accepted 23 August 1988.

0003–2409/89/080665+05 $03.00/0

© 1989 The Association of Anaesthetists of Gt Britain and Ireland

which may have important implications in the design of future equipment and patient management.

Design details

It was decided to produce a universal system with control provided for three gases, oxygen, air and nitrous oxide. Oxygen may be mixed with either air or nitrous oxide. A flow regulator is required for each gas and the system is controlled by a microcomputer. The gas mixer is shown diagrammatically in Figure 1. The earlier flow regulator consisted of eight low-power solenoid valves (Clippard EV-2M) mounted on a manifold and each connected by tubing to a bank of eight miniature needle valves. The solenoid valves and needle valves were both incorporated into a compact brass manifold to reduce the number of connexions. The earlier solenoid valves were retained but the opportunity was taken to use larger needle valves; those chosen were stainless steel cartridge valves (Fisher Controls Ltd). The larger needle valves selected performed closer to the ideal of a critical flow device.[3] One end of the manifold provides a high pressure inlet and the other a low pressure outlet. The adjustable spindles on the needle valves were locked by means of grub screws. The high pressure gas supplies for each regulator were taken via NIST (non-interchangeable screw thread) connectors (M and IE Ltd), mounted on the back panel, through high pressure tubing to each manifold. Nonreturn valves and filters were incorporated, and pressure tappings relayed the supply pressure for each gas to gauges mounted on the front panel.

Several safety features were incorporated into the design. The high pressure tubing was colour coded for the appropriate gases and the tubing connexions to spigots were crimped. A spring-loaded shuttle valve (Clippard FV-3) was fitted in the high pressure nitrous oxide line. The oxygen supply pressure activates this valve by means of a miniature piston (Clippard MPA-3). There is no possibility of contamination of the oxygen supply since the linkage between piston and shuttle valve is mechanical. The shuttle valve spring is adjusted so that the nitrous oxide is turned on only when the oxygen supply pressure exceeds 385 kPa, and cuts off when the oxygen pressure decreases below 325 kPa. The air supply was not affected. Two further tappings arise from the high pressure oxygen supply, one passes to a three-way selector switch via a needle valve (Platon Flowbits Ltd) both mounted on the front panel. This provides a manual oxygen override. The other oxygen tapping constitutes a fail-safe oxygen bypass and connects to a solenoid valve, normally open in the unpowered state. This then connects to an internal needle valve set at a fixed flow rate of oxygen of 6000 ml/minute. The flow from this valve then joins the combined outlets of the flow regulators. Thus, with no electrical power the flow-control valves close while this bypass valve remains open and a steady flow of oxygen of 6000 ml/minute is provided. The oxygen bypass valve closes, when the system is powered up, and the system is controlled by the microcomputer, unless in the manual setting. The low pressure outlets from the three flow regulators together with the oxygen bypass are all connected together by 8-mm diameter high pressure nylon tubing. The flow then passes through a three-way selector switch mounted on the front panel (Drallim Controls Ltd). This selector switch presents a low internal resistance and will withstand over 414 kPa gas pressure. It is used in this system to provide a manual/automatic changeover. From the selector switch the final output then passes to a simple, acrylic, Rotameter. This was approximately calibrated for air over the range 0 to 15 litres/minute and is used only to give an indication of flow. Following the flow meter a high pressure safety valve is fitted and this then connects to the 22-mm diameter tapered male outlet on the front panel. All connexions throughout the system are considered high pressure connexions.

Calibration of flow rate for each needle valve was accomplished by means of a 1550 ml bubble flow meter following a method originated by Barr.[6] This is a highly accurate technique but requires considerable skill to obtain a stable soap film at the higher flow rates. All the valves were

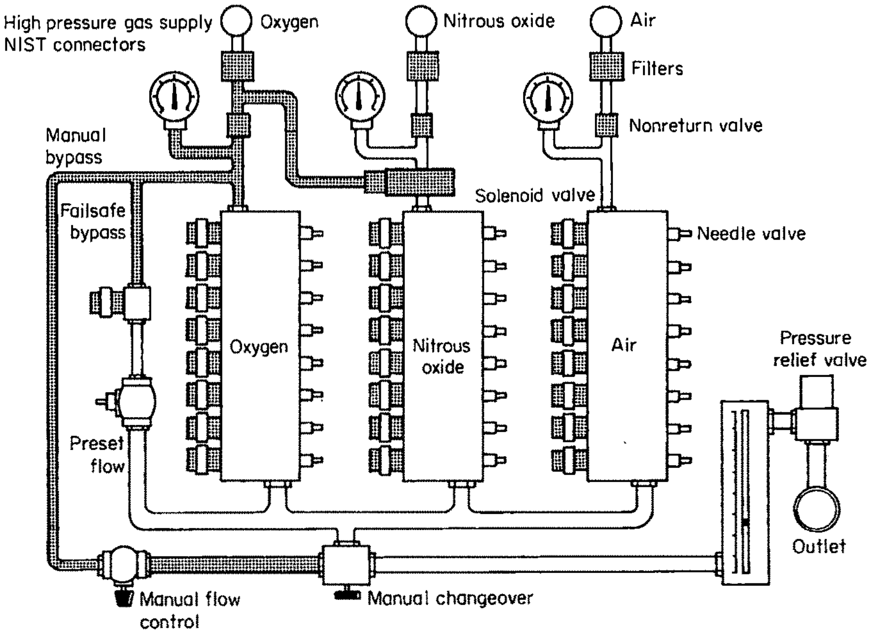
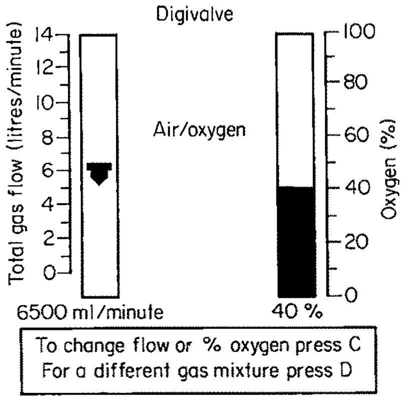


Fig. 1. Diagram of gas mixer.



To change flow or % oxygen press C
For a different gas mixture press D

Fig. 2. Computer screen display.

calibrated with an upstream pressure of 414 kPa gauge, corrected to 20°C; the outflow was corrected to 20°C and a pressure of one atmosphere. The valves were locked with a grub screw and checked again when the desired flow rate was obtained.

A BBC microcomputer (Acorn Computers Ltd) was used to control the mixer as in the earlier system. The link was via the 1 Mz Bus port using a similar interface as before.[7] The programming requirements this time incorporated a choice of oxygen concentration as well as flow rate. The control program was written in BASIC and the results displayed graphically show a floating bobbin for flow rate and a moving bar graph for oxygen concentration (Fig. 2). Constraints on both oxygen concentration and flow rate may be inserted into the program. The signal representing the flow rates for each gas are sent to the mixer every second but should an error develop in the program, the previous flow rates stored by the interface circuit are held and the program restarts ready to initiate new settings. The solenoid valves and the interface circuit have separate power supplies and the mains supply is filtered. Mains-borne interference is not uncommon in operating theatres and these precautions together with screening of the circuit board are an attempt to reduce this. The microcomputer used is unscreened and therefore vulnerable to air-borne interference. To date this has not been a problem.

System performance

The device was tested in two ways for mixtures of air/oxygen and repeated for nitrous oxide/oxygen. A range of flow rates were measured for different oxygen concentration settings, and oxygen concentrations measured for different flow rate settings. The behaviour of this type of system in response to changes in supply pressure, back pressure and long-term stability have been examined earlier.[1,8] It proved impractical to use Rotameters, since flow rates of gas mixtures were required, therefore a timed collection of gas was made into a 50-litre Douglas bag, previously evacuated to a constant pressure. The volume was then measured using a calibrated one-litre syringe and five measurements made for each flow rate. The mean value for each set of readings were taken. The minimum measurable volume with the syringe was 50 ml and to maximise accuracy a volume of at least 20 litres of gas was collected at the lower flow rates. Care was taken to keep the supply pressure for each gas at 414 kPa for each reading. The flow rates measured were corrected to ATP dry.

Table 1. Coefficient of variation of flowrate measurements as % of mean values for air/oxygen mixture at 5 preset oxygen concentrations.

	Preset flowrates ml/minute				
% oxygen	500	2500	5000	7500	10000
21	1.3826	0.7439	0.4200	0.4713	0.1021
30	0.7554	0.5530	0.1780	0.4255	0.1451
50	0.7233	0.4372	0.4476	0.6326	0.2677
80	1.6121	0.1797	0.2073	0.3841	0.2429
100	1.2159	0.5410	0.7392	0.2720	0.8944

To assess the performance in achieving desired oxygen concentrations, a Servomex 570A paramagnetic oxygen analyser was used over a range of flow rates. The analyser was calibrated against 100% nitrogen, 100% oxygen and room air. Four measurements were made at each setting and the mean taken. To condense the large number of measurements, two statistical evaluations were made. For each mean value the coefficient of variation expressed as a percentage of mean value was tabulated together with bias of the mean value expressed as a percentage of set point. There was little difference in the overall performance for the two gas mixtures, therefore only the results for air/oxygen, which are the more complex mixture, are shown (Tables 1–4). Several tests were performed over a period of 2 years and showed little variation in settings.

The mixer was also tested in a variety of hazardous situations such as oxygen supply failure, power failure, computer disconnexion and obstructed outflow. It behaved appropriately under these conditions.

Discussion

This paper describes a successful prototype microprocessor-controlled gas mixer and flow regulator built mostly from readily available, low cost components and capable of very accurate and repeatable outputs. It may lend itself to a variety of uses that require accuracy and microcomputer control.

Examination of the tabulated results for flow rates and oxygen concentration shows that coefficient of variation is provided as an estimation of repeatability and together with bias gives an overall picture of accuracy. The coefficient of variation for flow rate (Table 1) showed a nearly constant value, with the worst results at the lowest flow rates. The bias for flow rate (Table 2) tended to be positive and again increased with higher flow rates.

The oxygen concentration results (Tables 3 and 4) were even better than the flow rates. The coefficient of variation for oxygen concentration was uniform. The bias results for

Table 2. Bias of flowrate measurements as % of set point values for air/oxygen mixture at 5 preset oxygen concentrations.

	Preset flowrates ml/minute				
% oxygen	500	2500	5000	7500	10000
21	+2.80	+1.136	+1.764	+2.184	+0.702
30	+0.12	+0.88	+1.44	+1.2106	+0.282
50	+1.6	−0.904	+1.032	+1.712	+0.242
80	−0.52	−0.44	+1.064	+0.9146	+0.910
100	+3.64	+2.12	+1.312	+0.325	+0.508

Table 3. Coefficient of variation of oxygen concentration measurements as % of mean values for air/oxygen mixture at 5 preset flow rates.

Flow ml/ minute	Preset % oxygen values							
	30	40	50	60	70	80	90	100
500	0.339	0.356	0.181	0.215	0.074	0.065	0.0	0.0
2500	0.431	0.239	0.196	0.095	0.117	0.163	0.450	0.0
5000	0.505	0.144	0.189	0.136	0.071	0.101	0.091	0.0
7500	0.193	0.239	0.162	0.215	0.284	0.119	0.091	0.0
10 000	0.0	0.239	0.115	0.159	0.083	0.176	0.143	0.0

air/oxygen concentration (Table 4) demonstrate a feature of a digital system; the limits of resolution. In requesting an oxygen concentration the microcomputer takes into account the oxygen content of air and because of the minimum flow rate of 50 ml/minute, the computer must select the nearest concentration it can deliver. This is reflected in the bias results at some settings but is only a problem at lower flow rates and was not seen at these flow rates for the simpler mixture of oxygen/nitrous oxide.

Each flow rate comprises a combination of the flows through one to eight needle valves for each gas, and though it may be possible to analyse carefully the contribution from each valve, the quality of results already obtained does not require this for most purposes. Obviously the more precisely the valves are set, the more demanding is the test equipment required.

This type of device is sensitive to supply pressure in a linear manner. Pipeline supply pressures have a permissible variation of ± 5%[9] and should this prove unacceptable the effect may be compensated for in several ways. Pressure regulators may be used for each gas, calibrating the valves at a lower working pressure. Another method is to compensate for supply pressure changes in the software; supply pressure values could either be entered by hand or miniature pressure transducers tapped into each supply line and the pressure signal fed back to the control program. In practice the effect is experienced by all equipment supplied by pipelines and for general purpose use is not a major problem. To provide a safety margin the working software does not allow an oxygen concentration less than 30% with nitrous oxide. It is also mandatory that such a device be used with an oxygen monitor in clincal use.

This device is a prototype but some safety features were incorporated. The oxygen failsafe worked well but lacked a whistle. A nitrous oxide whistle could easily be provided but this does not meet modern requirements for a whistle based on a reservoir of oxygen. This calls for the addition of a small oxygen cylinder. The whole system could probably be miniaturised further, both from an electronic and mechanical point of view. Good quality components were used with long life expectancy. The solenoids are subjected to very little movement.

A contrasting method of using solenoids in gas mixing is described recently by Palayiwa *et al.*[10] in which solenoid valves rapidly open and close at changing pulse frequencies to vary the flow rate.

The high degree of linearity, accuracy, repeatability and microcomputer control of this device may provide a useful tool in many experimental situations. The mixer may be left unattended under preprogrammed control with a microcomputer both controlling and logging the results of an experiment. The device may also be viewed as a pneumatic digital-to-analogue converter and therefore produce simulations of sinusoidally varying oxygen concentration and flow rates, though attempts to do this confirmed the need for pulse damping devices.[10] In clinical use, trials are already under way in the use of this device in the feed-back control of end-tidal CO_2 and inspired oxygen concentration. Similar devices may well be incorporated into the anaesthetic machine.

Acknowledgments

The authors thank Professor C. Prys-Roberts for encouragement and discussion of the project and the Medical Physics Department for help in construction of the device. The equipment for the digital mixer was purchased with a grant from the Nuffield Foundation (Grant Number SCI/ 168/237) and computing hardware obtained from the Bristol and Weston Health Authority District Medical Research Committee (Project Grant 427).

Table 4. Bias of oxygen concentration measurements as % of set point values for air/oxygen mixture at 5 preset flow rates.

Flow ml/ minute	Preset % oxygen values							
	30	40	50	60	70	80	90	100
500	−2.845*	−2.027*	−1.556*	−1.721*	+0.110*	−0.230*	0.0*	0.0
2500	−0.167	+0.188	−0.051*	−0.245*	−0.143	+0.189*	−0.330*	0.0
5000	−0.917	+0.125	+1.050	+0.167	+0.536	+0.625	0.0	0.0
7500	−0.500	+0.063	+0.800	+0.250	+0.429	+0.656	0.0	0.0
10 000	0.0	+0.063	+0.100	+0.125	−0.211	+0.375	+0.389	0.0

*Set point different from desired.

500	29%	37%	53%	61%	68%	76%	92%
2500			49%	61%		79%	91%

References

1. Boaden RW, Hutton P. The digital control of anaesthetic gas flow. *Anaesthesia* 1986; **40:** 413–8.
2. Langill AW, Friedland H, Limbacher DL. New control valve accepts digital signals. *Control Engineering* 1969; **16:** 94–8.
3. Hutton P, Boaden RW. The performance of needle valves. *British Journal of Anaesthesia* 1986; **58:** 919–24.
4. Cooper JB, Newbower RS, Moore JW, Trautman ED. A new anaesthesia delivery system. *Anesthesiology* 1978; **49:** 310–8.
5. Lundsgaard JS, Einer-Jensen N, Juhl B. High pressure mixing of anesthetic gases based on a new principle. *Acta Anaesthesiologica Scandinavica* 1977; **21:** 308–13.
6. Barr G. Two designs of flowmeter and a method of calibration. *Journal of Scientific Instruments* 1934; **11:** 321–4.
7. Beverley P. Interface box for the Beeb. *Acorn User* 1983; May: 53–64.
8. Boaden RW, Hutton P. Digital computer control of gas flow. *British Journal of Anaesthesia* 1984; **56:** 799.
9. Department of Health and Social Security. Piped medical gases, medical compressed air and medical vacuum installations. *Hospital Technical Memorandum 1977*. No. 22 and Supplement.
10. Palayiwa E, Hahn CEW, Sugg BR, Lindsay-Scott D, Tyrell PJ. A microprocessor-controlled gas mixing device. *British Journal of Anaesthesia* 1986; **58:** 1041–7.

Anaesthesia, 1989, Volume 44, pages 670–671

HISTORICAL

A history of anaesthetic rooms

J. C. SONI AND D. A. THOMAS

Summary

The development of anaesthetic induction rooms since 1860 to the present day is outlined.

Key words

History; anaesthetic rooms.

The first general anaesthetics on both sides of the Atlantic were administered inside the operating theatre and on the operating table. Now, approximately 140 years later, anaesthetic rooms are used routinely for induction of anaesthesia in the United Kingdom and in many other countries. How did they originate? A diligent search of the literature has failed to reveal the origin of the concept of anaesthetic rooms.

The first mention of the use of such rooms for the induction of anaesthesia in the UK seems to have appeared in 1860 in a nonmedical publication, the *Cornhill Magazine.*[1] The anonymous author of the article wrote '... and while the patient is inhaling chloroform in an adjoining apartment ... when the unconscious patient is brought in by a couple of sturdy porters and laid upon the operating table'. In 1873 Tomes, a London dentist visiting Massachussetts General Hospital reported, 'The patient is etherised in a small anteroom adjoining the operating theatre...'.[2] In 1876 Osborn, a Surgical Registrar at St Thomas' Hospital, London wrote, 'Chloroform should be always administered, as it is at the hospital, in a small room adjoining the theatre, previously to the patient being brought in for operation, as he does not then become excited and is more quickly brought under the influence'.[3]

By 1937, the use of anaesthetic rooms was well established in the UK; a Ministry of Health publication[4] advised that there should be one anaesthetic room for each theatre with a floor area of 140 sq ft (13 sq m), direct entry from anaesthetic room to theatre and a separate exit from theatre. Also in 1937, a model of a proposed theatre suite, in which patients would be transported by overhead monorail between anaesthetic room and theatre, was shown at a Paris exhibition.[5]

Wheeler and Cassels of Chicago in 1947 supported the use of anaesthetic rooms on the grounds that '... the use of the operating room for anaesthetising ties it up unnecessarily and reduces the number of operations possible per room'. They report that some have advocated *two* anaesthetic rooms for each operating room![6] However, anaesthetic rooms were not provided in theatre designs published by the United States Public Health Service.[7]

In 1949, Ward[8] recommended a floor space of 196 sq ft (18.2 sq m). Ostlere[9] suggested in the following year that the anaesthetic room should be divided into two parts by a washable curtain. The patient should be wheeled into a compartment that looked as far as possible like an ordinary bedroom; it should be quiet, cool and dimly lit, with all equipment concealed behind the curtain. Hewer[10] considered the design and decor of anaesthetic rooms and described an anaesthetic room at St Bartholomew's Hospital where Ostlere's ideas were adopted; the walls and ceiling were decorated with paintings of a tranquil nature.[11] Steel[12] studied the reactions of patients to such paintings; he found that they were noticed and that their purpose was appreciated by the patients.

An important study on various aspects of theatre design in 1955[5] gave detailed recommendations for floor area and lighting intensity for various procedures in the anaesthetic room. An editorial in the *British Journal of Anaesthesia* in 1960[13] was devoted to the design of anaesthetic rooms and advised a minimum floor space of 224 sq ft (21 sq m), with more space in teaching hospitals. Essex-Lopresti[14] tried in 1963 to minimise the disturbance to the patient from changing trolleys, blankets and pillows by siting the anaesthetic rooms between the clean and dirty areas of the theatre suite. Also in 1963, the British Oxygen Company designed and built an anaesthetic room as part of their trade exhibit at the annual meeting of the Association of Anaesthetists of Great Britain and Ireland and invited opinions on design, size, decor, lighting and equipment.[15]

J.C. Soni, MB, BS, FFARCSI, Registrar, D.A. Thomas, FFARCS, Consultant, Department of Anaesthetics, Harold Wood Hospital, Gubbins Lane, Romford, Essex RM3 0BE.

Accepted 8 February 1989.

0003–2409/89/080670+02 $03.00/0

© 1989 The Association of Anaesthetists of Gt Britain and Ireland

Recommendations for the ideal anaesthetic room were made after comments had been received. It was stated at a meeting sponsored by the King Edward's Hospital Fund in 1965[16] that the need for anaesthetic rooms was an accepted part of National Health Service planning policy. One speaker regarded the anaesthetic room as part of the premedication and others suggested the provision of piped music, Victorian or Georgian decor, automatic doors and changing coloured lights.

Thus, the anaesthetic room, which originated as a small annexe to the theatre, has evolved as an integral part of operating theatre suites in the UK. However, their use has been abandoned in many countries and their disadvantages have resulted in reappraisal of their continued use in Great Britain. In an accompanying paper,[17] we report the results of a comparison of anxiety in patients who were anaesthetised either in an anaesthetic room or in the operating theatre.

Acknowledgments

We thank Dr D. Zuck for help and encouragement and Mrs J. Carter and Mrs B. New for secretarial help.

References

1. ANONYMOUS. Under Chloroform. *Cornhill Magazine* 1860; **1:** 499. (Reprinted in *British Journal of Anaesthesia* 1963; **35:** 330–3.)
2. TOMES CS. The administration of ether in America. *British Medical Journal* 1873; **1:** 297–8.
3. Reports of medical and surgical practice in the hospitals and asylums of Great Britain—chloroform and ether as anaesthetics. *British Medical Journal* 1876; **1:** 12–13.
4. Ministry of Health (1937). Departmental Committee on the cost of Hospital and other public buildings. Interim Report. HMSO. London.
5. *Studies in the functions and design of hospitals: The report of an investigation sponsored by the Nuffield Provincial Hospitals Trust and The University of Bristol.* London: Geoffrey Cumberlege, Oxford University Press, 1955.
6. WHEELER ET, CASSELS WH. Planning the operating room. *Anesthesiology* 1947; **8:** 567–78.
7. United States Public Health Service. Elements of the general hospital (revised edn.) *Hospitals* 1952; **26:** 79–132.
8. WARD R. *The design and equipment of hospitals.* London: Baillière, Tindall and Cox, 1949.
9. OSTLERE G. Aesthetics and anaesthetics; some observations on anaesthetic rooms. *Anaesthesia* 1950; **5:** 91–3.
10. HEWER CL. *Recent advances in anaesthesia,* 7th edn. London: Churchill, 1953: 404.
11. HEWER CL. Anaesthetic rooms. *British Medical Journal* 1955; **2:** 257.
12. STEEL GC. Decoration of the anaesthetic room: a study of patients' reactions. *British Medical Journal* 1959; **1:** 43–5.
13. Editorial. Safe working space. *British Journal of Anaesthesia* 1960; **32:** 95–6.
14. ESSEX-LOPRESTI M. The anaesthetist and theatre planning. *British Journal of Anaesthesia* 1963; **35:** 649–53.
15. LODER RE. The 'Harrogate' anaesthetic room; An investigation into anaesthetists' requirements. *Anaesthesia* 1964; **19:** 557–61.
16. A meeting at the Hospital Centre of the King Edward's Hospital Fund for London on 27 January, 1965. Anaesthetic room design. *Anaesthesia* 1965; **20:** 234–5.
17. SONI JC, THOMAS DA. Comparison of anxiety before induction of anaesthesia in the anaesthetic room or operating theatre. *Anaesthesia* 1989; **44:** 651–5.

Anaesthesia, 1989, Volume 44, pages 672–680

SPECIAL ARTICLE

Anaesthesia and substance abuse

P. R. WOOD AND N. SONI

Summary

Current practices in the abuse of illicit drugs in the United Kingdom are described with particular reference to their pathological effects and the implications for anaesthesia. Practical guidelines are given for the anaesthetic and peri- and postoperative management of addicts.

Key words

Analgesics; addiction.
Substance; abuse.

Drug abuse is as significant a problem in the United Kingdom as it is throughout the Western world and consequently anaesthetists will encounter patients with drug habits. Some background knowledge of the pattern of abuse is helpful since these patients present in both the acute and elective setting and recognition of potential problems may be difficult.

It is of interest that while almost every civilisation in recorded history has abused drugs, the nature, purity and route of administration of abused substances varies not only between, but also within, each culture. Furthermore, the patterns of drug abuse are affected by a wide range of influences and change continually. Consequently the patterns of abuse in the United States of America are not necessarily those of the United Kingdom and there are some marked differences. Nevertheless, in both countries the misuse of drugs has increased dramatically since the early 1980s. A precise analysis of the extent and nature of the street problem in the UK is impossible but trends are clear (Figs 1 and 2).

Heroin is the most serious problem in the UK. Assessments based on official notifications grossly underestimate the number of heroin addicts,[1] but there are at least 50 000 regular (daily) users. However, cocaine abuse also appears to have been increasing since 1980 if the quantities seized represent availability and use (Fig. 1); 1987 was a record year for seizures of this drug. The increased availability and expanding street market have resulted in lower prices so the drug is no longer restricted to the traditional affluent user and more widespread use in younger people is anticipated. Newer, highly purified preparations such as 'crack' which are common in the US, are not yet a problem in the UK. Other drugs commonly abused are dihyrocodeine (DF 118), dipipanone (diconal), barbiturates and increasingly, benzodiazepines. Amphetamines (the 'poor man's cocaine') and cannabis have both been readily available since the 1960s and their abuse persists; the misuse of amphetamines mirrors that of cocaine (Fig. 1). There is only sporadic abuse of the cyclohexylamine, phencyclidine (PCP, 'angel dust').

Sedative abuse is now recognised as a major problem in the community. This is not the result of illicit drug supply but rather a consequence of prescription in response to patient demand. The result is an estimated 500 000 dependent users in the UK[2] and now a growing street problem as these drugs are supplied illicitly. This is reflected in their recent addition (1986) to the list of controlled drugs (Class C).

The problem is not confined to the patient population, and addiction to volatile agents and abuse of narcotic drugs is a recognised hazard for doctors.[3,4] There are no hard data available in the UK about addiction in anaesthetists but some reporting may occur through the now established confidential voluntary help schemes. A large American study revealed a disturbingly high level of involvement by both trainee and senior anaesthetists.[5]

Definitions

The World Health Organisation (WHO) defines addiction in terms of its essential characteristics, which are as follows.

> A compulsive need to continue to take the drug and to obtain it by any means possible. Repeated exposure

---

P.R. Wood,* FFARCS, Senior Registrar, Northern Regional Rotation Scheme in Anaesthetics, N. Soni, FFARACS, Senior Lecturer, Magill Department of Anaesthesia, Westminster Hospital, Horseferry Road, London SW1.
*Present address: Department of Anaesthesia, South Cleveland Hospital, Middlesbrough, Cleveland TS4.

Accepted 27 January 1989.

0003–2409/89/080672+09 $03.00/0

© 1989 The Association of Anaesthetists of Gt Britain and Ireland

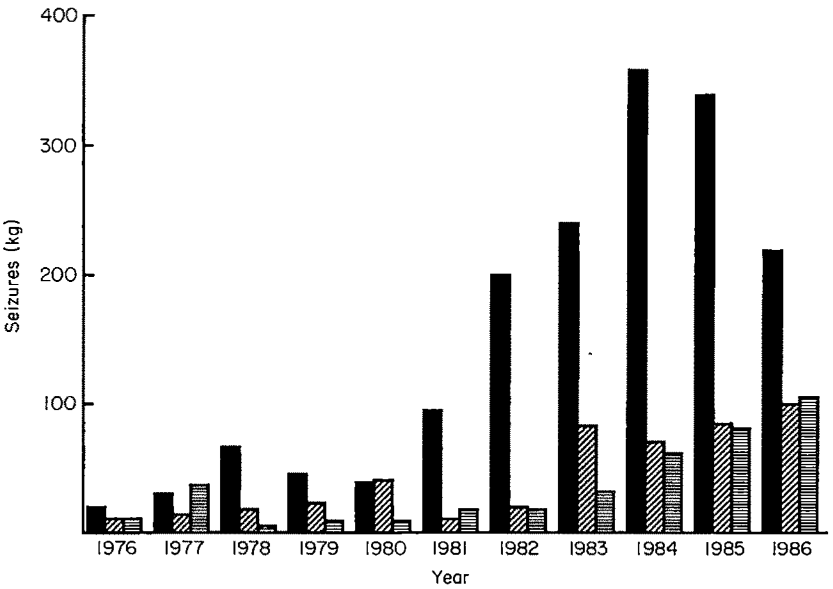


Fig. 1. Seizures by Police and Customs (UK) 1976–1986 (kg). Source: Statistics of the Misuse of Drugs, UK 1986. Home Office Statistical Bulletin: 29 September 1987 Issue 28/87. ■, heroin; ▨, cocaine; ▤, amphetamines.

leads to psychological dependence, that is, habituation.

Constant administration progresses to the development of a physical dependence in which the presence of the drug in the body is necessary for normal function.

A tendency to increase the dose as tolerance develops to the effects of normal concentrations of the drug.

An overall effect detrimental to the individual and society. The interpretation of this statement varies according to the substance and culture in question.

The physiological and biochemical mechanisms responsible for the state of addiction are not entirely understood. If a substance strictly fulfils the WHO's criteria then its withdrawal should produce a characteristic abstinence syndrome.

Mechanisms of dependence

Opioid-induced analgesia and dependence are discrete but closely associated pharmacological effects which may be controlled, in part, by opioid receptors,[6] but other mechanisms are also involved. These include the amino acid taurine which attenuates the abstinence syndrome in morphine-dependent mice possibly by antagonism to morphine-induced intracellular calcium deposition.[7] Several studies have suggested a role for gamma amino butyric acid (GABA) in morphine analgesia and dependence but the link remains unproven.[8]

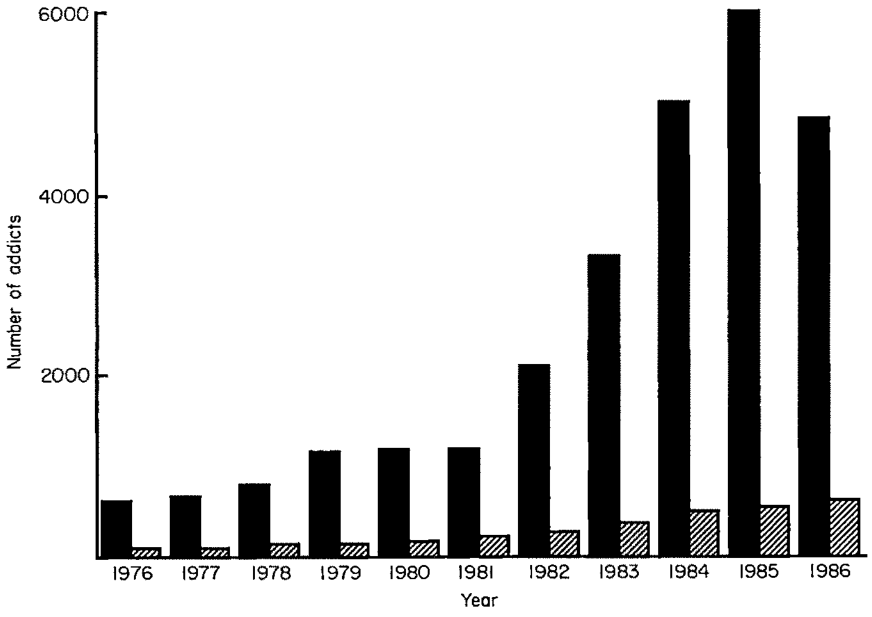


Fig. 2. Number of new addicts reported to the Home Office, 1976–1986. Source: Statistics of the Misuse of Drugs, UK 1986. Home Office Statistical Bulletin: 29 September 1987 Issue 28/87. ■, heroin; ▨, cocaine.

Long-term opiate administration may result in diminished production of endogenous opioid peptides (enkephalins) which are normally inhibitory to coexisting noradrenergic nuclei. Subsequent withdrawal is then characterised by sympathetic hyperactivity, the treatment of which has included thioridazine, diphenoxylate, beta blockers and more recently clonidine (*vide infra*).

Cocaine and amphetamine abuse is characterised by central dopaminergic stimulation. This action may also involve collateral neurotransmitters. Prolonged drug administration affects receptor sensitivity and is associated with a low level of dopamine metabolites.[9] Tricyclic antidepressants, anti-Parkinsonian drugs and bromocryptine have been used to treat cocaine abuse.

Specific drugs

Street heroin ('smack' 'H') is sold by the quarter. This suggests a content of 250 mg of heroin but in fact most heroin is sold in 100-mg aliquots and those are cut, so as to produce a mix of 40% heroin and 60% other colour-matched products (fillers). Heroin from different sources has various identifiable colours and the final colour will match its source colour. It is rare throughout the UK to obtain street heroin of less than 30% purity and it can increase to 60–70%. Purity rarely exceeds 7–8% in the US. Addicts normally take between one 'quarter' to a 'gram' daily. Phenobarbitone is often used to 'cut' the drug and its urinary detection (up to 4 days after the last dose) is used as a marker to identify methadone-maintenance patients who continue to take street drugs. Intravenous injection is most common but recently there appears to be an increase in the use of both nasal absorption ('chasing the dragon') and sublingual administration. This may reflect a growing awareness of the risks of AIDS and hepatitis but it is also because it reduces the risk of detection by identification of injection sites.

There is a growing population of young adults ('poly abusers') who abuse more than one drug: codeine, barbiturates and benzodiazepines are the most common.

Barbiturate abuse, usually the intermediate acting pento, quinal and quinal/amylobarbiturates, is both common and serious; severe dependency problems result. This is now also recognised of benzodiazepine abuse. Temazepam and diazepam are the usual agents and administration is often intravenous. Individual doses of 120–250 mg diazepam, up to a total of 600 mg daily are not unusual and some addicts reach up to 1500 mg a day. The result is an increasing number of deaths due to benzodiazepine overdose.

In London, cocaine and amphetamine abuse is rare amongst the dedicated heroin users, but in the US these agents are often mixed with opioids ('speedball') to antagonise unwanted opiate side effects. Cocaine in London (and this varies through the UK) is usually 55–65% pure (cut with sugar) and sold in 0.5–1-g quantities. It is normally absorbed by nasal snorting, but buccal absorption is also used. A typical 'snort' will use about 100 mg powder. It is a potent vasoconstrictor and high dose chronic abuse can cause septal ulceration. A small number of users inject it intravenously where its effects are immediate but persist for a few minutes only. Large doses cause sympathetic overstimulation and there is a high risk of both cardiovascular and central nervous system effects that include cardiovascular collapse and convulsions.[10] The use of highly purified forms such as 'crack' (which can be smoked) is not widespread but their potential danger is in accelerated dependence, which is an understated problem. The resultant abstinence syndrome has signs and symptoms that meet the criteria for true withdrawal.[10] Cocaine can, amongst its other effects, prolong the action of suxamethonium.[11]

Amphetamine abuse also leads to sympathetic overstimulation as well as to bizarre mental states which are often described as paranoid schizophrenia. It is taken orally, by sniffing or intravenous injection (speed). Recent administration may be difficult to recognise before operation and the sympathetic stimulation may cause intra-operative cardiovascular problems.[12,13] This is distinct from the problems of chronic abuse where catecholamine depletion is the probable cause of the observed reduction in anaesthetic requirements.[9,14] The abuse of over-the-counter stimulants ('look alikes') is an established problem in the US[15,16] and a potential future difficulty for the UK.

Abuse of lysergic acid diethylamide (LSD) and other hallucinogens is less common than in the 1960s and '70s, and the predicted threat in this country from PCP (angel dust) has not materialised. Pharmacological actions of the hallucinogens include a sympathomimetic action which can hinder assessment of cardiovascular changes during anaesthesia. LSD prolongs suxamethonium block and delays metabolism of both ester type local anaesthetics and narcotic analgesics. It also possesses some intrinsic anticholinesterase activity.[17]

Solvent abuse is increasing amongst adolescents. Most are under 15 years of age and co-abuse of other illicit drugs is common.[18] The clinical features of sniffing mimic acute alcohol intoxication. Physical dependence is rare but tolerance and psychological dependence can develop.[18] Chronic physical symptoms include cardiomyopathy[19] and irreversible neurological changes.[18] The interaction between hydrocarbons and catecholamines is recognised as cardiodepressant and exercise-induced arrhythmias are implicated in sudden cardiac deaths.[20] The combination of solvent-induced hypoxia, hypokalaemia and alcohol ingestion is arrhythmogenic.[19]

Cannabis (marijuana) has a long history of experimentation by man, for both therapeutic and social reasons. Its complex pharmacology[21] ensures that traditional views of its abuse/therapeutic potential are continuously being revised.[22]

The active substances have a wide range of pharmacological actions; most of the observable psychotropic effects are due to 9 tetrahydrocannabinol, THC. The mechanisms of action remain unknown but include both anaesthetic and analgesic effects. Recent administration may have additive effects with concomitantly administered premedicants. On induction the duration of action of both ketamine and thiopentone is prolonged and during anaesthesia there is an additive effect with volatile agents.[23,24]

Cardiovascular effects include tachycardia which is potentiated by both atropine and adrenaline. There is an increased peripheral blood flow, from possible beta adrenergic stimulation.[25] Hypo or hypertension can result.

Central nervous system effects include dysphoric and panic reactions with occasional severe psychosis. Withdrawal after chronic use can produce an abstinence syndrome similar to that seen with benzodiazepines and hypnotics.[21,22] Controversy persists over the possibility of harmful long-term neurological effects.

Table 1. Signs and symptoms of substance abuse.

Substance	
1. Narcotics	Euphoria (most marked with heroin). Conscious level ↓→coma. Pinpoint pupils with overdose. Respiratory depression. Hypotension. Constipation. Chronic respiratory dysfunction (see Table 2).
2. Cocaine and amphetamines	Sympathetic stimulation, excitement, delirium, hyperreflexia, tremors, convulsions, mydriasis, sweating hyperpyrexia. Labile blood pressure; hypertension. Hallucinations (tactile = 'cocaine bugs'; visual = 'snow lights')→psychosis. Exhaustion and coma with overdose.
3. Hypnotics; benzodiazepines and barbiturates	Central nervous system depression. Mood calming. Overdose = respiratory depression and coma. Hypothermia and cardiovascular depression
4. Hallucinogens: phenycyclidine derivatives. LSD	Altered perception and judgement. High doses may progress to toxic psychosis. Sympathomimetic and feeble analgesic effects. Phencyclidine produces dissociative anaesthesia with increasing doses.
5. Volatile solvents	Altered perception. Euphoria. Overdose produces coma with progression similar to effects of general anaesthesia. Respiratory and cardiovascular depression. Ventricular arrhythmias from halogenated hydrocarbons.
6. Cannabis	Effects variable but dose related. Euphoria. Occasional anxiety and panic reactions. Rarely psychosis. Pulse rate ↑. Blood pressure ↑↓. Chronic use may induce poor memory and decreased motivation.

Clinical uses are restricted at present. Certain derivatives are effective as antiemetics in malignant disease but side effects are prominent.[26]

'Designer drugs' are a particularly worrying new aspect of drug abuse because a wide range of active pharmacological agents may be employed and often the user does not know the ingredients. This poses significant problems in diagnosis and management of the acute crises seen with some of these drugs. It was reported from the US at first in 1979, but sporadic abuse of such drugs has since occurred in London.

The association of alcohol and drug abuse was previously of minor significance although the two were not mutually exclusive. However, concurrent alcohol and drug abuse is growing as a serious problem in young 'polyabusers'. It is usually employed to antagonise unwanted effects from other drugs, or as a substitute when the usual agent of abuse is not available, and so it may be abused by methadone addicts who are being weaned from their narcotic dependency. The subject of alcohol and anaesthesia has been reviewed in detail by Edwards and Mosher.[27] Table 1 gives specific information on clinical drug information.

Presentation to anaesthetists

There are many reasons why a substance abuser may present for anaesthesia or intensive care. Apart from specific effects particular to their drug or habit, many of the hazards are related to unclean techniques, overdose or trauma.

Drugs concealed inside the body may also necessitate radical care. In 1986 13% of heroin and 11% of cocaine detected by the UK customs was smuggled internally. Ruptured containers result in massive overdose.

Table 2 details possible reasons for emergency or inpatient care.

Physical examination

Pathological effects of substance abuse may be local at the point of administration or develop systemically, including coincident infections. Relevant physical findings are listed in Table 2.

Nasal absorption of drugs produces few physical signs. Sinusitis and ulceration of the nasal mucosa are seen with cocaine but septal perforation is rare.[9,37] 'Glue sniffers' rash' may be seen on the face in some cases of solvent abuse.[18] The needle marks of intravenous abuse will occasionally be seen although this is becoming less common. Narcotic users classically demonstrate hypertrophic pigmented scars (tracks) over peripheral veins in contrast to cocaine injections whose fresh injection sites are characterised by multiple ecchymoses.[37] Injection sites may be obscured by tattoos and the femoral and neck vessels should not escape inspection while the range of sites is limited only by imagination.

Peripheral oedema may exist as a consequence of needling (Table 2) but if generalised, hepatic disease, or in heroin addicts the nephrotic syndrome,[38] may be responsible.

Unusual neurological and psychiatric presentations such as the severe extrapyramidal disorders[34,35] produced by 'designer drugs' can be confusing, but the presence of localising signs from coincident head injury must not be missed.

A general examination is necessary after looking for specific indications of abuse. With intravenous abusers this should include any evidence of liver disease. Ophthalmological examination should be thorough since very occasionally candidiasis may be identified by changes in visual acuity with lesions visible in the fundi. The cutaneous and oral manifestations of HIV disease should also be sought.[39] Septicaemia should be suspected if a pyrexia of unknown origin exists. Cardiomyopathy must be excluded in cases of heavy alcohol abuse.[27]

Investigations before anaesthesia

Haemoglobin and urea and electrolyte estimations are important, as is a glucose estimation. A 25% incidence of chronic anaemia has been reported in one American series of methadone maintenance patients.[40]

Liver function tests are frequently abnormal in narcotic addicts.[40,41] The fillers used to cut pure product are the usual cause in the UK. Hepatitis is a special consideration with HIV infection and is discussed below.

A chest X ray is important because of the association of

Table 2. Pathology related to substance abuse.

Pathology	Presentation	Comments
1. Results of acute intoxication or overdose	Primary = Central nervous system stimulation or depression: fitting, coma. Hyperthermia from stimulant abuse.[28] Arrhythmias, BP crises (hyper/hypotension). Respiratory depression: hypoxic fits.	Overdose commonest cause of death in heroin addicts (diagnosis = coma, meiotic pupils and respiratory rate 2–6 litres/minute).
	Pulmonary oedema with heroin intoxication	Common postmortem finding.
	Secondary = Trauma, including head injuries. Pancreatitis.	Localising signs important in assessment.
2. Acute medical and surgical problems associated with abuse habits[29, 30]	As venous injection sites lost intra-arterial injections initiated → spasm, mycotic and false aneursyms. Vessel rupture. Extravastion of i.v. injections → lymphatic and venous obliteration = 'puffy hand' syndrome.	
	Subcutaneous injections → abscesses + necrotising fascitis; 'skin popping' i.v. injections (mainlining) → circulatory complications, including acute and subacute endocarditis (right and or left sided). Systemic emboli from left sided disease valve destruction → cardiac failure (high mortality). Candida septicaemia.	Tricuspid valve pathology + pulmonary infarcts with positive blood cultures in absence of pre-existing venous disease is highly suggestive of narcotic addiction.
	Heroin addicts have recurrent chest problems—asthma common. Aspiration likely when acutely intoxicated. Tuberculosis occurs in heroin addicts. Respiratory disease (especially pneumocystis pneumonia) commonest presentation of HIV disease.[31]	Often asthmatic since childhood.
	Heroin addicts may present with pseudo obstruction. Mechanical obstruction from swallowed cocaine or heroin: 'body packers', 'stuffers and swallowers'.[32, 33]	May have signs of acute intoxication. Massive overdose may result.
	Septic techniques may produce tetanus. Psychiatric illness, mood disorders. Cerebral emboli/abscess from endocarditis.	Differential diagnosis of tetanus = Parkinson's disease from 'designer drugs'.[34, 35]
3. Related surgical and obstetric disease	Dental caries common in narcotic addicts. Old trauma may require orthopaedic or plastic correction. Obstetric care: late presentation. Pre-eclampsia ↑ in heroin addicts.[36]	

aspiration and recurrent infection with intoxication. Hilar lymphadenopathy occurs in intravenous narcotic abusers and may be a reflection of the fillers (including quinine, sugar, starch and brick dust) used in the street drugs. Septic pulmonary emboli can produce multiple interstitial infiltrates ('mainliner's lung')[29] which can occur without evident right-sided endocarditis. A chest X ray may demonstrate cardiomyopathy due to alcohol[27] or solvent abuse.[19] The electrocardiogram is abnormal in over 50% of narcotic abusers where a prolonged QT interval may be of relevance in cases of sudden death.[42]

In suspected 'body packers' (Table 2) an abdominal X ray is mandatory and can be of prognostic significance.[32,33]

Plasma screening for paracetamol, barbiturates and salicylates is a rapid process that may help in the management of intoxicated patients, and urinary screening for morphine can be performed in 2 hours. Other results take longer but urine and plasma samples should always be retained to allow late analysis if necessary.

Infection risk (hepatitis and AIDS)

Between 1980 and 1984, 1597 cases of acute hepatitis B occurred in UK intravenous drug abusers (24% of all reported cases).[43] Eighty percent of drug-abuse-associated infections are in men. Reported figures were lower by 1987 for reasons not yet clear, but there is a new threat in Hepatitis Delta (HDAg).[44]

This agent was first reported in 1979 among Italian patients with chronic liver disease, many of whom were drug users. It is a morphologically distinct hepatitis agent independently transmitted from Hepatitis B, but dependent on the latter for replication. It can produce fulminant hepatitis with rapid progression to chronic active hepatitis and cirrhosis. Infection is by direct parenteral transmission and in the USA 20–53% of intravenous drug abusers are infected.

An epidemic of Delta disease has occurred in Dublin since 1980 where 41% of Hepatitis B surface antigen-positive drug abusers have Delta markers. The Delta virus can suppress Hepatitis B antigen production and give negative results in standard screening tests, so that drug abusers should be separately tested for this agent. Coincidental HIV infection may reactivate latent Delta infection.[44] Vaccination against Hepatitis B is the only current means of prevention of infection with Delta.

AIDS was first reported in drug abusers in the US in 1981. Currently between 5 and 20% of American intravenous drug abusers are infected with HIV and account for 75% of all their heterosexually transmitted cases of

AIDS.[45] In Europe 14% of cases are intravenous drugs users although there is wide national and regional variation. In Scotland 55% of people positive for HIV have abused drugs intravenously as compared to about 8% in the rest of the country. In one central London health district reviewed by the authors, 18% of the present methadone maintenance patients are HIV positive. (None of these are positive for Hepatitis B.) The drug dependency unit studied considered any patient injecting drugs since 1976 to be at possible risk from HIV infection. From 1979 the risk is considered 'definite' and from 1982 the situation is described by others as the heterosexual epidemic.[45]

Many London addicts have either stopped, or attempted to reduce the dangers of sharing dirty needles and syringes.[46,47] The possibility that HIV infection acquired by heroin addicts may prove to be unusually aggressive[48] is not so far supported by clinical experience.

Detailed reviews of the influence of Hepatitis B[49] and AIDS [50] on anaesthetic practice are available but local infection control policies should be adhered to.

The theatres[49,50]

The management of risk patients for either Hepatitis or HIV is well delineated in the DHSS guidelines.[51,52] The minimal number of personnel should handle the patients and all should be protected by gowns, gloves and overshoes. Goggles or a visor should also be worn if there is a likelihood of blood being splashed or sprayed. Resheathing of needles should be avoided. Needle puncture should be minimised and the use of three-way taps and injection ports which do not require needle puncture should be encouraged. Disposable equipment should be used whenever possible and placed in well-marked buckets or plastic bags for disposal. Care in the identified group minimises risk and the main danger is from carelessness in the nonidentified groups.

Premedication and pain relief

The same principles for premedication apply to this population as to normal patients, but due consideration must be given to the background drug abuse. The two main pitfalls are overdose or withdrawal. It must be remembered that even in hospital, some addicts are adept and maintain their illicit supplies. Care must be taken to avoid dual administration but it is equally important to avoid withdrawal problems.

Heroin addicts may present with a background of illicit street use, or more rarely may be under supervision on a methadone-maintenance programme. The following principles are important in peri-operative management.

> The addict's usual total daily dose should be discovered. This must then be considered a 'physiological requirement' and it (or an equipotent dose of another narcotic) becomes the minimal daily requirement irrespective of additional considerations of acute pain relief, background analgesic or sedation. Analgesic requirements will be excessive and withdrawal precipitated if this principle is not observed. This principle must not be neglected if regional techniques are employed.
>
> Street addicts are notorious for exaggeration about their doses, in the hope of obtaining increased quantities of the drug. Overdose can easily result if their true tolerance is exceeded. Therefore when acute analgesia is necessary the time of the addict's own last dose may be important (the half-life of heroin is normally 4–6 hours).
>
> Narcotic addicts should be offered the assistance of specialists in drug dependency and their narcotic doses stabilised before operation if surgery is not urgent.
>
> The normal daily dose can be given intramuscularly early on the day of elective operation in methadone stabilised addicts. Premedication and peri-operative analgesia is then given in addition.
>
> The late postoperative period (48 hours) is a suitable time to convert the total daily narcotic dose to oral methadone after uncomplicated emergency surgery on a street addict. This requires supervision by a drug dependence specialist and assumes a compliant patient.

Postoperative analgesia may be a problem. The use of intermittent injections is likely to produce peaks and troughs with consequent demands for both increased frequency and size of dosage. Infusions are therefore better, but have the risk of increased self administration. They should only be used in high dependency areas.

Heroin and methadone are equipotent. 'Conversion' doses are shown; all values are approximate because potency of street heroin varies.

0.25 g street heroin = 20 mg methadone substitute.
0.25–0.50 g street heroin = 40 mg methadone substitute.
0.50–1.00 g street heroin = 60 mg methadone substitute.

Methadone has a half-life of up to 90 hours and is given as a single daily dose. An occasional patient may be a 'cured' narcotic abuser. The agonist/antagonist type of analgesics are theoretically attractive in this situation because they are less habit forming. However, their use in the addict using narcotics is potentially hazardous since withdrawal may be precipitated. The addict's former doses in the assessment of analgesic requirements are irrelevant because as withdrawal is completed tolerance rapidly disappears and a return to a former 'maintenance' dose can be fatal.

Anaesthetic technique

Local techniques may be rewarding if the method is suitable for postoperative analgesia because it may reduce the possibility of abuse of narcotics in this period. The tendency of general anaesthesia to produce hypotension in narcotic addicts,[53] which is a possible manifestation of withdrawal, can also be avoided with regional blockade.

Regional analgesia may not, unfortunately, be practical for various reasons. Narcotic addicts often are very uncooperative with therapeutic needles and in dental surgery a lowered pain tolerance and relative failure of regional analgesia is described, even after large doses of local anaesthetics.[54] The more needles in use the greater the risk to medical staff of transmissible hazards from needlestick injuries. Sepsis can be a contraindication,[55] as will any coagulation disorder due to hepatic dysfunction. Any preexisting peripheral neuropathy should be clearly documented.

Addition of adrenaline to local anaesthetic agents can potentiate cannabis-induced tachycardia.[25] The dose of local anaesthetic must be reduced in the presence of liver disease or significant hypoalbuminaemia.

The normal routine of establishing intravenous access can create major problems in the narcotic addict. Many veins (including central vessels) will be thrombosed or show evidence of phlebitis. A cooperative patient will usually readily indicate the vessel most likely to produce success but often an addict will protect their own reliable source of access. The use of central veins may provide inadvertent instruction in access to vessels.

General anaesthesia

Intravenous induction is usually smooth in narcotic addicts and provided that their normal narcotic requirements are met, cross tolerance is not a major problem during the maintenance phase of anaesthesia.

Cross tolerance to sedative agents may be a serious problem in benzodiazepine abusers, some of whom take massive doses by therapeutic standards. Induction may require large doses of barbiturate, and awareness in the maintenance phase of anaesthesia is always a possibility. The problems can be worsened by coexistent alcohol abuse.[27] The degree of tolerance in amphetamine and cocaine addicts will alter according to the timing of the most recent acute episode of heavy usage (*vide infra*).

The position of nitrous oxide is interesting. There is evidence that it is an agent of abuse, possibly through a direct interaction with the endogenous opioid system,[56] and prolonged exposure may lead to tolerance when used in anaesthesia.[57] It has been used to treat opiate (*vide infra*) and alcohol addiction,[58] but it is not clear if it has a role in postoperative analgesia for narcotic addicts.

Inhalational agents help to achieve a balanced anaesthetic, but the choice may be influenced by the patient's abuse history. Halothane is at a disadvantage because it sensitises the myocardium to the effects of catecholamines (endogenous or otherwise) and is contraindicated in active liver disease. Enflurane sensitises the myocardium to a lesser degree and undergoes less hepatic metabolism. Its proconvulsant property may be a relative contraindication in abusers of central nervous system stimulants. Isoflurane is on theoretical grounds, a more suitable choice.

Withdrawal features and treatment

Symptoms of opiate withdrawal appear 8–12 hours after the last dose and include fatigue, weakness, restless sleep ('yen'), yawning, lacrimation, rhinorrhea, perspiration, fever, diarrhoea and dehydration. Pilo-erection produces gooseflesh ('cold turkey'). Symptoms peak at 48–72 hours and continue for 7–10 days if untreated.[59] Acute withdrawal is rarely fatal unless precipitated by the injection of an opiate antagonist in an addict who has not overdosed.

The symptoms are a result of sympathetic hyperactivity and are modified by the alpha-2 agonist clonidine.[60,61] This drug is now established in the clinical treatment of heroin withdrawal. Cramps, sweating and abdominal symptoms are particularly relieved, but postural hypotension can be a problem.

Acute withdrawal is usually treated with methadone alone. Ten milligrams is given orally and after a delay of 20 minutes a further 10 mg is given and every 10 minutes thereafter. A favourable response is judged by a decrease in pulse rate and a return to a normal blood pressure. The same dose of methadone may be given intramuscularly or subcutaneously or diluted and given intravenously in small boluses.

Barbiturate withdrawal is potentially life threatening if abrupt or misdiagnosed. The sequence of anxiety, weakness, insomnia, headache and tremors progress after 24 hours to hypotension, vomiting and grand mal fits.[59] Management using a pentobarbitone substitution technique is described, but benzodiazepines are equally effective. Abuse of benzodiazepines is also associated with a barbiturate-type withdrawal response.[62] Abrupt withdrawal can result in major convulsions, and if completed prolonged psychological problems may result.[63] Treatment involves the reintroduction of the drug with a slow reduction in dose over a period of days to weeks.

Withdrawal from the stimulants cocaine and amphetamine can be difficult to recognise. Some abusers enter a prolonged sleep phase ('crash') (up to 24–48 hours) at the end of a period of chronic heavy usage followed by hunger, depression, delirium, delusions and hallucinations. This is thought to represent catecholamine depletion,[9,17] the opposite mechanism to that of acute intoxication. The syndrome should be left to run its course, but severe depression may warrant expert psychiatric help.

Abstinence from hallucinogenic drugs is rarely a problem. Classically 'trips' are separated by a period of days, as tachyplylaxis occurs to the CNS effects.[17,64] Psychotic episodes occur on rare occasions in susceptible individuals, days or months after ingestion.[17] Benzodiazepines are appropriate treatment if abstinence of cannabis produces symptoms in a chronic user. The importance of correct identification and treatment of delirium tremens[27] is such that this condition must be a differential diagnosis in any withdrawal of uncertain aetiology.

Intensive therapy

Addicts may require admission to intensive care for postoperative management or directly as a complication of their habit. Postoperative management of both analgesia and sedation is often difficult. Determination of the maintenance levels of opiate from the patient is notoriously unreliable and it may be necessary to give opiates until the requisite therapeutic effect is achieved. Supplementation with other sedative agents may help reduce the total dosage. This may be quite a considerable dose but the ITU is not the place to attempt weaning from an established habit. The use of infusions to produce stable levels of opiate rather than intermittent administration is probably preferable.

There are a wide range of others causes for admission to ITU. This group of patients present as a consequence of trauma, including head injury, more frequently than the general population. Another common cause of admission with altered sensorium, is overdosage. Both these diagnoses must be considered on admission, and if drug overdosage is suspected thorough screening for the type of agent is necessary.

Sepsis is common in these patients and while infected injection sites, abscesses and pneumonia are usual, exotica such as right-sided endocarditis, candida ophthalmitis, and septicaemia should also be remembered. A complication of treatment occasionally seen in the ITU is withdrawal, as patients are, for example, weaned from automatic lung ventilators. Agitation, sweating, tachycardia, tachypnoea and labile blood pressure in a fulminant form can produce a worrying differential diagnosis. A small dose of opiate produces a dramatic resolution of the problem, which is otherwise a diagnosis of exclusion.

Another major consideration in ITU management is that of Hepatitis B or HIV infection. Department of Health guidelines should be followed.[51,52] ITU personnel should be immunised against Hepatitis B.[65]

Acknowledgments

The authors are grateful for the considerable assistance given by Dr G. Dhanani, Consultant Psychiatrist, St Stephen's Hospital, Fulham, and Officers of the Metropolitan Police Drugs Squad in the preparation of this article.

References

1. Hartnoll R, Mitcheson M, Lewis R, Bryer S. Estimating the prevalence of opioid dependence. *Lancet* 1985; **i:** 203–5.
2. Ashton CH. Dangers and medico-legal aspects of benzodiazepines. *Journal of the Medical Defence Union* 1987; **3:** 6–8.
3. Spiegelman WG, Saunders L, Mazze RI. Addiction and anesthesiology. *Anesthesiology* 1984; **60:** 335–41.
4. Herrington RE, Benzer DG, Jacobson GR, Hawkins MK. Treating substance-use disorders among physicians. *Journal of the American Medical Association* 1982; **247:** 2253–7.
5. Ward CF, Ward GC, Saidman LJ. Drug abuse in anaesthesia training programs. A survey: 1970 through 1980. *Journal of the American Medical Association* 1983; **250:** 922–5.
6. Ling GSF, MacLeod JM, Lee S, Lockhart SH, Pasternak GW. Separation of morphine analgesia from physical dependence. *Science* 1984; **226:** 462–4.
7. Contreras E, Tamayo L. Effects of taurine on tolerance to and dependence on morphine in mice. *Archives International Pharmacodynamics* 1984; **267:** 224–31.
8. Buckett W.R. The role of GABA in analgesia and drug dependence. *Reviews in Pure and Applied Pharmacological Sciences* 1981; **2:** 115–41.
9. Gawin FH, Ellinwood EH. Medical Progress. Cocaine and other stimulants. Actions, abuse and treatment. *New England Journal of Medicine* 1988; **318:** 1173–81.
10. Gossop M. Beware cocaine. *British Medical Journal* 1987; **295:** 945.
11. Jatlow P, Barash PG, Van Dyke C, Radding J, Byck R. Cocaine and succinylcholine sensitivity: a new caution. *Anesthesia and Analgesia* 1979; **58:** 235–8.
12. Michel R, Adams AP. Acute amphetamine abuse. Problems during general anaesthesia for neurosurgery. *Anaesthesia* 1979; **34:** 1016–9.
13. Samuels SI, Maze A, Albright G. Cardiac arrest during cesarean section in a chronic amphetamine abuser. *Anesthesia and Analgesia* 1979; **58:** 528–30.
14. Johnston RR, Way WL, Miller RD. Alteration of anesthetic requirement by amphetamine. *Anesthesiology* 1972; **36:** 357–63.
15. Whitehouse A. Should sympathomimetics be available over the counter? *British Medical Journal* 1987; **294:** 1308.
16. Pentel P. Toxicity of over-the-counter stimulants. *Journal of the American Medical Association* 1984; **252:** 1898–1903.
17. Jenkins LC. Anaesthetic problems due to drug abuse and dependence. *Canadian Anaesthetists' Society Journal* 1972; **19:** 461–77.
18. Sourindrhin I. Solvent misuse. *British Medical Journal* 1985; **290:** 94–5.
19. Boon NA. Solvent abuse and the heart. *British Medical Journal* 1987; **294:** 722.
20. Bass M. Sudden sniffing death. *Journal of the American Medical Association* 1970; **212:** 2075–9.
21. Jones RT. Cannabis and health. *Annual Review of Medicine* 1983; **34:** 247–58.
22. Ashton CH. Cannabis: dangers and possible uses. *British Medical Journal* 1987; **294:** 141–2.
23. Stoetling RK, Martz RC, Gartner J, Creasser C, Brown DJ, Forney RB. Effects of delta 9-tetrahydrocannabinol on halothane MAC in dogs. *Anesthesiology* 1973; **38:** 521–24.
24. Vitez TS, Way WL, Miller RD, Eger EI. Effects of delta 9-tetrahydrocannabinol on cycloprane MAC in the rat. *Anesthesiology* 1973; **38:** 525–7.
25. Beaconsfield P, Ginsburg J, Rainsbury R. Marihuana smoking. Cardiovascular effects in man and possible mechanisms. *New England Journal of Medicine* 1972; **287:** 209–12.
26. Bateman DN, Rawlins MD. Therapeutic potential of cannabinoids. *British Medical Journal* 1982; **284:** 1211–2.
27. Edwards R, Mosher VB. Alcohol abuse, anaesthesia and intensive care. *Anaesthesia* 1980; **35:** 474–89.
28. Rosenberg J, Pentel P, Pond S, Benowitz N, Olson K. Hyperthermia associated with drug intoxication. *Critical Care Medicine* 1986; **14:** 964–9.
29. Geelhoed GW, Joseph WL. Surgical sequelae of drug abuse. *Surgery, Gynecology and Obstetrics* 1974; **139:** 749–55.
30. Organ CH. Surgical procedures upon the drug addict. *Surgery, Gynecology and Obstetrics* 1972; **134:** 947–52
31. Millar AB. Respiratory manifestations of AIDS. *British Journal of Hospital Medicine* 1988; **39:** 204–15.
32. McCarron MM, Wood JD. The cocaine 'Body Packer' syndrome. Diagnosis and treatment. *Journal of the American Medical Association* 1983; **250:** 1417–20.
33. Lancashire MJR, Legg PK, Lowe M, Davidson SM, Ellis BW. Surgical aspects of international drug smuggling. *British Medical Journal* 1988; **296:** 1035–7.
34. Langston JW, Ballard P, Tetrud JW, Irwin I. Chronic Parkinsonism in humans due to a product of meperidine-analog synthesis. *Science* 1983; **219:** 979–80.
35. Williams A. MPTP Parkinsonism. *British Medical Journal* 1984; **289:** 1401–2.
36. Connaughton JF, Finnegan LP, Schut J, Emich JP. Current concepts in the management of the pregnant opiate addict. *Addictive Diseases: An International Journal* 1975; **2:** 21–35.
37. Mittleman RE, Wetli CV. Death caused by recreational cocaine use. An update. *Journal of the American Medical Association* 1984; **252:** 1889–93.
38. Kilcoyne MM, Gocke DJ, Meltzer JI, Daly JJ, Thomson GE, Hsu KC, Tannenbaum M. Nephrotic syndrome in heroin addicts. *Lancet* 1972; **i:** 17–20.
39. Farthing CF, Brown SE, Staughton RCD. *A colour atlas of AIDS and HIV disease,* 2nd edn. London: Wolfe Medical, 1988.
40. Rubenstein RB, Spira I, Wolff WI. Management of surgical problems in patients on methadone maintenance. *American Journal of Surgery* 1976; **131:** 566–9.
41. Stimmel B, Vernace S, Tobias H. Hepatic dysfunction in heroin addicts. The role of alcohol. *Journal of the American Medical Association* 1972; **222:** 811–2.
42. Lipski J, Stimmel B, Donoso E. The effect of heroin and multiple drug abuse on the electrocardiogram. *American Heart Journal* 1973; **86:** 663–8.
43. Polakoff S. Incidence and Prevalence Rates in the UK. In: *Hepatitis B in the UK. Proceedings of conference at the RSM, London.* Mark Allen, 1986: 4–7.
44. Shattock A. Delta—a growing problem? In: *Hepatitis B in the UK. Proceedings of conference at the RSM, London.* Mark Allen, 1986: 19–23.
45. Moss AR. AIDS and intravenous drug use: the real heterosexual epidemic. *British Medical Journal* 1987; **294:** 389–90.
46. Ghodse AH, Tregenza G, Li M. Effect of fear of AIDS on sharing of injection equipment among drug abusers. *British Medical Journal* 1987; **295:** 698–9.
47. Strang J, Hunt S, Johns A. Syringe exchange schemes. *British Medical Journal* 1988; **297:** 200.
48. Hendrickse RG, Maxwell SM. Heroin addicts, AIDS, and aflatoxins. *British Medical Journal* 1988; **296:** 1257.

49. Waterson AP. Hepatitis B as a hazard in anaesthetic practice. *British Journal of Anaesthesia* 1976; **48:** 21–4.
50. Lee KG, Soni N. AIDS and anaesthesia. *Anaesthesia* 1986; **41:** 1011–6.
51. Department of Health and Social Security. Guidance to surgeons, anaesthetists, dentists and their teams in dealing with patients infected with HTLV III. DHSS; CMO (86) 7 April 1986.
52. Nursing Services: Riverside Health Authority. HIV infection—operational policies and procedures April 1988.
53. Mark LC, Marx GF, Arkins RE, Kepes ER, Radnay PA, Ravin MB, Steen SN. Hypotension during anesthesia in narcotic addicts. *New York State Journal of Medicine* 1966; **66:** 2685–6.
54. Scheutz F. Drugs addicts and local analgesia—effectivity and general side effects. *Scandinavian Journal of Dental Research* 1982; **90:** 299–305.
55. Gomar C, Luis M, Nalda MA. Sacro-ilitis in a heroin addict. A contra-indication to spinal anaesthesia. *Anaesthesia* 1984; **39:** 167–170.
56. Gillman MA. Nitrous oxide, àn opioid addictive agent. Review of the evidence. *American Journal of Medicine* 1986; **81:** 97–102.
57. Smith RA, Winter PM, Smith M, Eger EI. Tolerance to and dependence on inhalational anesthetics. *Anesthesiology* 1979; **50:** 505–9.
58. Lichtigfeld FJ, Gillman MA. The treatment of alcoholic withdrawal states with oxygen and nitrous oxide. *South African Medical Journal* 1982; **61:** 349–51.
59. Jaffe JF. Drug *addiction and drug abuse.* In: Goodman LS, Gilman AG, Rall TW, Murad F, eds. *The pharmacological basis of therapeutics,* 7th edn. New York: Macmillan, 1985: 532–81.
60. Ghignone M, Quintin L, Duke PC, Kehler CH, Calvillo O. Effects of clonidine on narcotic requirements and hemodynamic response during induction of fentanyl anesthesia and endotracheal intubation. *Anesthesiology* 1986; **64:** 36–42.
61. Gold MS, Pottash ALC, Extein I, Kleber HD. Clonidine in acute opiate withdrawal. *New England Journal of Medicine* 1980; **302:** 1421–2.
62. Petursson H, Lader MH. Benzodiazepine dependence. *British Journal of Addiction* 1981; **76:** 133–45.
63. Ashton H. Benzodiazepine withdrawal: an unfinished story. *British Medical Journal* 1984; **288:** 1135–40.
64. Elliott HW. Effects of street drugs on anaesthesia. *International Journal of Clinical Pharmacology and Biopharmacy* 1975; **12:** 134–40.
65. Zuckerman AJ. Control and management of infections. Hepatitis B. *Hospital Update* 1988; **14:** 1389–1400.

Anaesthesia, 1989, Volume 44, pages 681–683

Forum

The attitudes of junior anaesthetists to research

A survey

D. G. Gaylard, BSc, FFARCS, Lecturer, Department of Anaesthesia, St Thomas' Hospital, London, J. M. Lamberty, FFARCS, Senior Registrar, Department of Anaesthesia, Southmead Hospital, Bristol.

Summary

A survey was undertaken to investigate aspects of research work undertaken by junior anaesthetists. Two hundred and ninety-five junior anaesthetists were surveyed. Forty-seven percent of respondents were involved actively in research activities at the time of the survey, although 57% of senior house officers and registrars and 30% of senior registrars would not attempt to acquire publications except to improve their curriculum vitae. Few had received any formal training in research methods. The significance of these findings is discussed with regard to current training opportunities.

Key words

Education; junior anaesthetists.
Research.

It is now generally accepted that the completion and publication of research projects are requirements for junior anaesthetists who apply for senior registrar and consultant posts. The 'bottleneck' between registrar and senior registrar grades has forced registrars to look for additional ways to improve their curriculum vitae. The majority of applicants for senior registrar posts have wide pre- and post-fellowship anaesthetic experience; this may include a period of training abroad or at a specialist centre in the UK. In addition, many trainee anaesthetists undertake research projects in the belief that publications have become a measure on which interview shortlists and appointments are made. Concern has been expressed that this may result in a situation in which the quantity rather than the quality of such work may become the important factor.[1]

We were interested in a number of aspects of research work undertaken by junior anaesthetists and investigated this by means of a questionnaire.

Method

The questionnaire was distributed to junior anaesthetists in the South West Region and the London teaching hospitals. The South West Region was studied in late 1987 and early 1988 and the London area in mid-1988. Two hundred and ninety-five questionnaires were sent, to be returned anonymously. We tried to ensure that all junior doctors in each region were sent a questionnaire. Inevitably not all were included because of movement of junior staff and the late return of some papers.

The questions were arranged in four sections as follows: basic personal details including the number of years spent at each level of training; details of past and present research and whether published/accepted or in preparation; opinions regarding the importance of research for promotion at each grade, and future research intentions; and the availability of advice and formal teaching of research skills. The full questionnaire is shown in Table 1.

Results

The overall response rate was 46%, better in the South West Region (58%) than in London (39%) and senior registrars were better respondents than other grades: senior registrars (SR) 73%, registrars 38%, and senior house officers (SHO) 37%. Registrars had spent an average of 1.8 years as SHO, and SRs an average of 3.4 years as registrar. There was considerable individual variation and we did not seek details of the time spent as an SHO or other grade before entering anaesthesia.

The mean ages and the average number of publications of respondents at each grade are shown in Table 2. The total of three publications for all the SHOs excludes two SHOs in the London region who had over 12 publications each; these publications resulted from full time research posts completed before the individuals entered the specialty of anaesthesia and were excluded from the table because we considered that they did not reflect the average SHO.

Forty-seven percent of respondents were involved actively in research at the time of the survey (SRs 76%, registrars 37%, SHOs 15%). The percentage of SRs involved in research did not differ greatly between the regions but more SHOs and registrars participated in research in London than the South West Region (38% compared with 20%).

Table 3 shows the percentage of anaesthetists who regard publications as essential or very important for promotion to the grades indicated. Fifty-seven percent of SHOs and registrars would not attempt to acquire publications if they did not need them for their curriculum vitae; this figure was 30% for SRs.

The expectations of involvement with research as a con-

Accepted 27 February 1989.

0003–2409/89/080681 + 09 $03.00/0

© 1989 The Association of Anaesthetists of Gt Britain and Ireland

Table 1. The questionnaire.

1. Age:
2. Current post:
   Senior House Officer Registrar Senior Registrar
3. Years in post as:
   Senior House Officer Registrar Senior Registrar
4. How many papers of yours are:
   Published In press In preparation/submitted
   Letters:
   Case reports:
   Articles:
   Reviews:
   Others:
5. Are you actively involved in any research?
   YES/NO
6. Do you think publications are necessary for your CV when applying for the position of:
   Registrar Senior Registrar Consultant
   Essential:
   Very important:
   Moderately important:
   Unimportant:
7. If you did not need publications for your CV would you still attempt to acquire them?
   YES/NO
8. As a consultant do you see yourself involved with research?
   Definitely:
   Probably:
   Unlikely:
   No:
9. Can you name your department's clinical tutor?
   YES/NO
10. Has anyone discussed research with you?
    YES/NO
11. Do you feel there is someone available for advice on research projects?
    YES/NO
12. Have you had any formal teaching about the problems and approach to starting a research project?
    YES/NO

Table 2. The mean ages in years and the average number of publications at each grade.

	Senior House Officer	Registrar	Senior Registrar
Mean age, years	28.3	29.8	33.9
Average number of publications	3 (total)	1	5.9

Table 3. Percentage of anaesthetists who regarded publications as essential or very important for promotion.

	Opinions of		
Promotion to	Senior House Officer	Registrar	Senior Registrar
Registrar	10%	7%	4%
Senior Registrar	72%	65%	76%
Consultant	82%	93%	84%

Table 4. Numbers (%) of each grade who thought that they would be involved with research as a consultant.

	Senior House Officer	Registrar	Senior Registrar
Definitely	6 (15)	3 (7)	11 (20)
Probably	13 (33)	14 (33)	17 (31)
Possibly	12 (31)	14 (33)	21 (38)
Unlikely	7 (18)	9 (21)	5 (9)
No	1 (3)	3 (7)	1 (2)

Table 5. Numbers of papers in each category for SHOs.

	Published	In press	In preparation
Letters	9	—	3
Case reports	2	—	4
Articles	25	—	—
Reviews	4	1	4
Others	2	—	—

Table 6. Numbers of papers in each category for Registrars.

	Published	In press	In preparation
Letters	15	4	5
Case reports	4	1	11
Articles	6	4	12
Reviews	5	1	3
Others	6	2	4

Table 7. Numbers of papers in each category for Senior Registrars.

	Published	In press	In preparation
Letters	58	12	3
Case reports	40	4	18
Articles	109	23	62
Reviews	13	4	6
Others	62	5	6

sultant are shown in Table 4. Tables 5–7 show the number of publications, and their nature, for the three grades of trainee anaesthetist.

Only 60% of trainees could name their department's Faculty (now College) Tutor; those in London were better informed (76%) than their colleagues in the South West (50%). Only 36% of registrars in the South West could name their Faculty Tutor. A senior colleague had discussed research intentions with most registrars and senior registrars and 90% of respondents felt that advice was available to them if they requested it. Only 17% had received any formal teaching in research.

Discussion

About half of the junior anaesthetists surveyed were involved actively in research; most registrars and senior registrars had published something, usually without formal teaching and often only because they believed that it was necessary for their curriculum vitae. Indeed, only about half of the senior registrars overall thought that they might definitely or even probably be committed to any research as a consultant.

These publications may be of variable worth; publication of original research in a journal which subjects submissions to peer review deserves greater credit than a case report in a local society journal or a letter. Aitkenhead[2] has suggested that the increased quantity of published research in recent years has not been matched by an increase in quality. While we agree that the provision of research training in this country is in need of improvement, our survey suggests that many anaesthetists in training wish to continue in clinical anaesthesia without being forced into research. It has been noted previously by Skinner[3] that judgment of applicants for clinical posts on their research abilities is an unreasonable means of selecting clinicians since there is little proof that achievement in research correlates with clinical skills. This pressure could certainly contribute to work of questionable quality.[4]

Alternatives are required if an increase in the number of publications as a result of increased competition for posts is considered undesirable. A reduction in the number of career anaesthetists to prevent the bottleneck between registrar and senior registrar grades is one possibility, and such a move has been urged in surgery where the problems are even more immediate.[5] Production of a maximum of three publications[6] or the completion of a thesis, as suggested by Spence,[7] may encourage a higher quality of work and might allow clinical anaesthetists to obtain a greater proportion of their training time in clinical anaesthesia.

Sixty-eight percent of junior anaesthetists thought that publications are essential or very important when applying for SR posts. However, it is often difficult for the junior grades to obtain time in which to undertake research. The fellowship examination makes great demands on time and teaching commitments. An increasing number of teaching hospital posts now include district general hospital rotations where the facilities for research may not be as accessible as in the teaching centres. The rotations inevitably mean that less time is spent in any one department, and this makes the completion of a research project even more difficult. Many of our respondents stated spontaneously that time was a major problem in carrying out research. This situation appears unchanged since 1980 when a survey by Barham *et al.*[8] noted many complaints about lack of time for research and study. There appears also to be a lack of formal training in research. Aitkenhead[2] noted that only one fifth of original papers from institutions in the United Kingdom published in *Anaesthesia* or the *British Journal of Anaesthesia* in 1984 and 1985 had an academic co-author. We consider that college tutors should be involved with all aspects of training, including research and the fact that many juniors did not know their tutor may indicate room for improving this important area of teaching.

References

1. Halsey MJ. Editorial. Science and anaesthesia. *Anaesthesia* 1985; **40:** 733–4.
2. Aitkenhead AR. Editorial. Does anaesthetics research need training? *British Journal of Hospital Medicine* 1986; **35:** 287.
3. Skinner AC. Fraud in medicine. *British Medical Journal* 1988; **296:** 574.
4. Lock S. Fraud in medicine. *British Medical Journal* 1988; **296:** 376–7.
5. Salaman JR. Achieving a balance—a time for action. *British Medical Journal* 1988; **296:** 717–8.
6. Wallwork J, Wells FG. Pressure of research on junior staff. *British Medical Journal* 1986; **292:** 1139.
7. Spence AA. Scientific writing and peer review. *British Journal of Anaesthesia* 1981; **53:** 783–4.
8. Barham C, Thompson MA. Senior registrar rotations. A survey of rotational arrangements. *Anaesthesia* 1980; **35:** 607–10.

Anaesthesia, 1989, Volume 44, pages 683–685

Epidural anaesthesia for day care surgery

A retrospective study

V. J. Sarma, FFARCSI, Consultant, Piteå General Hospital, 941 28 Piteå, J. Lundström, MD, Chairman, Department of Anaesthetics, Skellefteå General Hospital, 931 86 Skellefteå, Sweden.

Summary

The records of 682 patients who received epidural anaesthesia for day care surgery were reviewed. The advantages and disadvantages of this form of anaesthesia is discussed. No major complications were recorded.

Key words

Anaesthesia, regional; epidural.
Surgery; day care.

There is a growing demand for the performance of more surgical procedures on a day care basis. Regional anaesthetic techniques for day care surgery are popular because they allow early and painless return of function after surgery. The most suitable techniques are those which allow a rapid return of reflexes and which can be adminis-

---

Accepted 26 November 1988.

tered easily. It is also important that the technique has a low risk of complications and that these should be apparent before the patient is discharged from the unit.

We have used epidural anaesthesia for day care surgery since 1969 in our District General Hospital,[1] and since then over 3000 epidurals have been performed on outpatients. However, computerised records of only 682 patients who had day care surgery under epidural anaesthesia in the last 3.5 years are available.

We have reviewed the merits and problems involved with epidural anaesthesia in this setting.

Methods

Epidural anaesthesia was administered to 682 day care patients who had surgery below the umbilicus. There were 319 males and 363 females and they ranged from 18 to 82 years in age. All the patients were considered fit for day care surgery and had no major systemic disorders. Patients below the age of 18 years do not normally receive local anaesthetic blocks in our day care unit. No premedication was prescribed. The skin and subcutaneous tissue were infiltrated, in all cases, with local anaesthetic solution before the epidural space was located by the loss of resistance technique.

The anaesthetist who performed the block chose the local anaesthetic, the dose, and whether to use a continuous or a single shot technique. The drugs used were bupivacaine 0.5% or mepivacaine 2% with adrenaline (5 μg/ml) in all cases. The patients received intravenous fluids, vasopressors such as ephedrine and sedatives or opioids during the course of the operation according to the advice of the anaesthetist in charge. The dermatomal level of the block was assessed by drawing an ice cube along the body from below upwards. All the epidurals were performed by residents and regular anaesthetic staff, and only residents who had performed at least 50 epidurals were allowed to perform the blocks on the day care unit.

The patients remained in bed after surgery, until the anaesthetic had worn off and they had regained full motor and sensory function in their legs. All were tested for return of perianal sensation and proprioception in the foot before walking was allowed.[2] They were also encouraged to demonstrate the ability to micturate before they were discharged from the unit.

The patients were allowed to leave after a final examination by one of the anaesthetic staff. They were advised to stay at home until at least the next morning and special instructions about movement around the house were given.

All the patients were advised to contact the hospital in case of any unusual difficulties. A provision was made for the admittance of any patient unfit to be discharged.

Table 1. Types of operations performed under epidural anaesthesia in the day care unit ($n = 682$).

Varicose vein surgery (unilateral or bilateral)	324
Arthroscopy (unilateral or bilateral)	181
Arthroscopy + menisectomy	33
Minor orthopaedic procedures (hallux valgus correction, metatarsal osteotomies removal of intramedullary nails, tendon repair, ganglion removal etc.)	62
Urological procedures (Bladder tumour resection, orchidopexy, phimosis correction, hydrocoele operation, lithotripsy, ureterolithotomy, urethrotomy)	65
Minor surgical procedures (Femoral hernia repair, removal of rheumatic nodules, skin grafting, excision of skin tumors etc.)	17

Table 2. Minor complications during 682 epidural anaesthetics.

	Number
Failed epidural (no effect at all)	6
Block wore off before surgery was completed	18
Blood pressure decrease >25%	26
High level of block ($>T_4$)	7
Difficulty in performing the block (> than one attempt at locating the epidural space)	23
Chest pain	1

Table 3. Response to questionnaire ($n = 109$).

	Yes	No	Don't know
Was the anaesthetic satisfactory?	89 (81.7%)	15 (13.8%)*	5 (4.5%)
Was it unpleasant to be awake during the operation?	11 (10.1%)	96 (88%)	2 (4.5%)
Will you have the same anaesthetic again if needed?	79 (72.5%)	12 (11%)	18 (16.5%)

*Experienced pain during the performance of the epidural	6
Experienced pain during the operation	8
Was unpleasant to be awake during the operation	6
Had residual paraesthesia for over a week in the feet	1

Results

A single shot technique was used on 292 occasions. The duration of the operations ranged from 0.5 to 3 hours and 90.8% of the patients were discharged within 5 hours of the end of the operation. Sixty three (9.24%) were admitted after their operation; 53 (7.77%) of these for surgical reasons because more than the intended operation had been performed.

Two patients (0.3%) had dural punctures and both needed a blood patch for relief of postspinal headache. Five patients (0.73%) had difficulty in micturition for up to 6 hours after the administration of the epidural, but all were able to micturate normally within 8 hours.

One patient had chest pain and was admitted for observation, but cardiac-enzymes study revealed no infarction. Another patient had prolonged motor and sensory weakness which lasted more than 6 hours from the start of the epidural. This woman received a continuous epidural anaesthesia for bilateral varicose vein surgery using plain bupivacaine 85 mg. Full recovery occurred 9.25 hours after the epidural was instituted; the upper level of the block was T_4 and there were no adverse postepidural sequelae in this patient after recovery.

The most common complication was backache, which

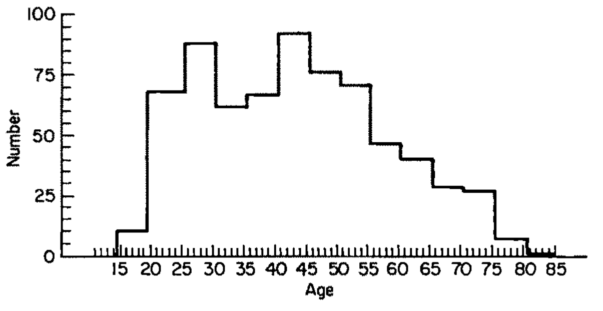


Fig. 1. Total patients, 682; age range, 18 to 82 years; mean age, 43.27 years.

was present in 64 patients (9.34%). The pain varied in severity and lasted on average for 2 days, although one patient had pain for a week. Treatment with heat, physiotherapy and mild analgesics resolved this problem in all patients. The first 113 patients in this group were asked to fill in a questionnaire about the epidural and 109 of them replied, a response rate of 96.5%.

Discussion

Any anaesthetic technique suitable for day care surgery should be easy to administer and provide the essential features of rapid outpatient recovery, namely alertness, ambulation, analgesia and alimentation. The absence of these and the presence of pain and vomiting are the most frequent anaesthesia-related reasons for the admission of the outpatient.[3] Thus somnolence, pain and nausea, which are considered minor side effects of general anaesthesia, are important complications for the outpatient.

Epidurals were administered in day care units[1,4-6] and in pain clinics on an outpatient basis[7,8] with satisfactory results. Other techniques, such as spinal intradural anaesthesia, were not found to be suitable in a day care setting, because even when a 25-gauge needle is used, the incidence of postspinal headache in 51 young male patients was reported to be 37.2%.[9] Field and plexus blocks in the lower extremity are not easy to perform and frequently require multiple injections and the use of large volumes and dosage of local anaesthetic.

Backache seems to be a prominent complaint after epidural anaesthesia, but is well known after all forms of anaesthesia.[10] The incidence of backache following spinal anaesthesia is reported to be between 2 and 25%.[11] The exact aetiology is unknown in most cases. Various factors such as relaxation of the back musculature, trauma to the ligaments or vertebrae at the site of the puncture, and a possible psychological overlay that arises from the fact that a lumbar procedure was performed, have been suggested.[11]

Epidural haematoma that results in prolonged motor and sensory block is a serious complication of this form of anaesthesia and can occur even in the absence of any anticoagulant therapy.[12] We perform a CAT scan routinely in all cases of prolonged block that last over 6 hours, to rule out this complication.

The main drawback with epidural anaesthesia in the day care unit appears to be the additional time required to perform it, but with adequate planning and facilities for separate induction areas, the time spent is no greater than it would take to induce and recover a patient after general anaesthesia. Aromaa[5] and Bridenbaugh[6] have reported a faster recovery, and fewer postoperative side effects following epidural than after general anaesthesia. Ambulation was safe, and orthostatic hypotension was not a problem once there was full return of perianal sensation and proprioception in the foot.[2] Meridy,[3] in a retrospective study of 1553 day care surgical patients, found that neither the type of surgery nor the age of the patient affected the duration of recovery or the rate of complications. Thirty-five of our patients (5.13%) were over 70 years of age. They reacted no differently to the epidural when compared with the rest of the group.

Conclusions. Epidural anaesthesia was used in 682 outpatients and was found to be a safe and effective technique; only two patients (0.3%) had a dural tap and developed postspinal headache. No serious postepidural sequelae were noted and most patients (90.76%) were discharged within 5 hours after the operation.

References

1. Kjellgren A, Lundström J, Ygge H. Extraduralanestesi i ambulant praxis. *Särtryck ur Opuscula Medica* 1969; **14:** 181–8.
2. Pflug AE, Aashiem GM, Foster C. Sequence of return of neurological function and criteria for safe ambulation following subarachnoid block. *Canadian Anaesthetists' Society Journal* 1978; **25:** 133–9.
3. Meridy HW. Criteria for selection of ambulatory surgical patients and guidelines for anaesthetic management: a retrospective study of 1553 cases. *Anesthesia and Analgesia* 1982; **61:** 921–6.
4. Bridenbaugh LD. Regional anaesthesia for outpatient surgery—a summary of 12 years' experience. *Canadian Anaesthetists' Society Journal* 1983; **30:** 548–52.
5. Aromaa U. Anaesthesia for short-stay varicose vein surgery. *Acta Anaesthesiologica Scandinavica* 1977; **21:** 368–73.
6. Bridenbaugh LD, Soderstrom RM. Lumbar epidural block anesthesia for outpatient laparoscopy. *Journal of Reproductive Medicine* 1979; **23:** 85–6.
7. Crawford ME, Andersen HB, Augustenborg G, Bay J, Beck O, Benveniste D, Larsen LB, Carl P, Djernes M, Eriksen J, Grell AM, Henriksen H, Johansen SH, Jørgensen HOK, Møller IW, Pedersen JEP, Ravlo O. Pain treatment on outpatient basis utilizing extradural opiates. A Danish multicentre study comprising of 105 patients. *Pain* 1983; **16:** 41–7.
8. Zenz M, Piepenbrock S, Tryba M. Epidural opiates: long-term experiences in cancer pain. *Klinische Wochenschrift* 1985; **63:** 225–9.
9. Flaatten H, Raeder J. Spinal anaesthesia for outpatient surgery. *Anaesthesia* 1985; **40:** 1108–11.
10. Middleton MJ, Bell CR. Postoperative backache: attempts to reduce incidence. *Anesthesia and Analgesia* 1965; **44:** 446–8.
11. Moore DJ. Complications of regional anaesthesia. In: Bonica, JJ ed. *Regional Anaesthesia.* Philadelphia: F.A. Davies, 1969: 218–51.
12. Bromage PR. *Epidural Analgesia.* Philadelphia: W.B. Saunders, 1978: 654–715.

Anaesthesia, 1989, Volume 44, pages 685–687

Temazepam or midazolam for night sedation. A double-blind study

J. Irjala, MD, Staff Anaesthetist, Department of Anaesthesiology, Turku Municipal Hospital, Turku, J. Kanto, MD, Reader in Anaesthesia and Clinical Pharmacology, M. Salonen, MD, Staff Anaesthetist, Department of Anaesthesiology, Turku University, Central Hospital, Turku, Finland.

Summary

The effects of oral temazepam (20 mg), oral midazolam (15 mg) and a placebo were compared for night sedation on the evening prior to surgery in a double-blind study. Patients in the placebo group had significantly worse sleep than those in the temazepam ($p = 0.004$) or midazolam groups ($p = 0.04$). There was no significant difference between the two drug groups, nor between the residual effects of the three treatments. Temazepam appears to be somewhat more effective than the ultrashort-acting midazolam in pre-operative transient insomnia.

Key words

Hypnotics; benzodiazepines, midazolam, temazepam.

Routine use of hypnotics is acceptable to treat transient insomnia before operation. A good night's sleep is essential to ensure a smooth induction of anaesthesia.[1,2] Benzodiazepines are widely used.[1,2] Midazolam among different derivatives appears to have the shortest duration of action,[3] whereas that of temazepam lasts around 7 to 8 hours without significant residual effects.[4] Nowadays the use of derivatives with ultrashort action, like midazolam,[5] is increasing and therefore we have evaluated the usefulness of midazolam, temazepam and a placebo as night-time sedatives before elective surgery. The secondary aim was to compare the residual effects of the drugs just before operation by using several subjective and objective variables.

Methods

The study was conducted as a double-blind, double-dummy, parallel group comparison. Patients were randomly allocated to receive a single oral 15-mg dose of midazolam (Dormicum, Roche) a 20-mg dose of temazepam (soft gelatine capsule, Normison, Wyeth) or placebo (tablet and capsule) at 2200 hours. No premedication was given on the morning of surgery.

All the patients were ASA class 1 or 2 and those on long-term treatment with psychoactive drugs, or who had taken benzodiazepines during the past 14 days, were excluded. Pregnant patients, patients with hypersensitivity to benzodiazepines, and those with myasthenia gravis or narrow angle glaucoma were also excluded. Data on sleep, residual sedation, apprehension, excitement, dizziness, effect on salivation, setting up infusion, emetic effect and headache were collected in the operating theatre on 4-graded scales[6-8] between 0800 and 1000 hours on the morning of operation. The patients were operated on under spinal or epidural analgesia. Sixteen of them had combined regional and general anaesthesia.

Differences between groups in age, weight and height were tested using one-way analysis of variance (source of variation = drug). The subjective and objective measurements taken on 4-graded scales in the operating theatre were analysed using Kruskal–Wallis non-parametric analysis of variance.

Results

Data were available for 90 patients, 30 of whom received midazolam (Table 1). There were no significant differences in the distribution of age, sex, weight and height between the three drug groups.

The subjective effects after treatment of the three drugs are summarised in Figure 1 and Table 2 (setting up of infusion was assessed by the anaesthetist, J.I.).

There was a significant difference in the sleep experienced by the patients in the three groups (Kruskal–Wallis test, $p = 0.013$). There was no significant difference between the active groups (Mann–Whitney *U* test), but the patients in the placebo group had significantly worse sleep than those

Table 1. Patient data. Values expressed as mean (SD).

	Midazolam ($n = 30$)	Temaxepam ($n = 32$)	Placebo ($n = 28$)
Male : female ratio	12 : 18	12 : 20	13 : 15
Age, years	43.2 (7.6)	40.4 (8.7)	38.6 (11.1)
Males			
Weight, kg	79.6 (9.0)	82.3 (10.8)	79.9 (9.6)
Height, cm	176.3 (6.9)	176.8 (5.3)	177.1 (4.4)
Females			
Weight, kg	68.4 (11.1)	67.9 (11.0)	64.9 (8.9)
Height, cm	162.7 (3.4)	162.8 (4.9)	160.3 (5.1)

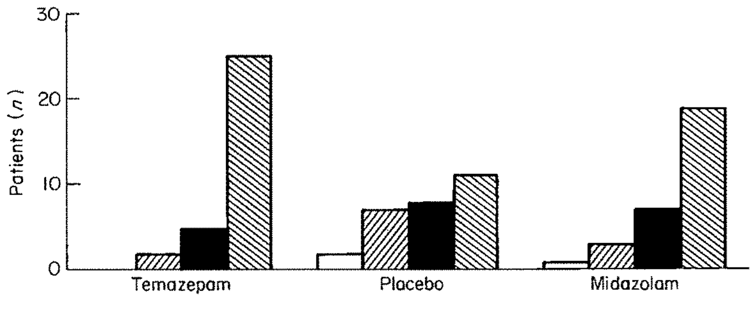


Fig. 1. There was no significant difference in the quality of sleep produced with temazepam 20 mg or with midazolam 15 mg, but the patients in the placebo group reported a significantly worse sleep than those in the temazepam ($p = 0.004$) or midazolam groups ($p = 0.04$). □, poor; ▨, fair; ■, moderate; ▧, good.

Accepted 22 February 1989.

Table 2. Effects of temazepam 20 mg, midazolam 15 mg and placebo given the night before surgery on various scores before operation.

	Temazepam	Placebo	Midazolam
Sedation			
marked	0 (0.0%)	0 (0.0%)	0 (0.0%)
moderate	0 (0.0%)	5 (17.9%)	1 (3.3%)
slight	10 (31.2%)	7 (25%)	7 (23.3%)
none	22 (68.8%)	16 (57.1%)	22 (73.3%)
Apprehension			
absent	19 (59.4%)	13 (46.4%)	19 (63.3%)
slight	7 (21.9%)	13 (46.4%)	7 (23.3%)
moderate	5 (15.6%)	2 (7.9%)	3 (10.0%)
marked	1 (3.1%)	0 (0.0%)	1 (3.3%)
Excitement			
none	9 (28.1%)	6 (21.4%)	7 (23.3%)
slight	18 (56.3%)	15 (53.6%)	16 (53.3%)
moderate	4 (12.5%)	6 (21.4%)	6 (20.0%)
marked	1 (3.1%)	1 (3.6%)	1 (3.3%)
Dizziness			
none	25 (78.1%)	21 (75.0%)	21 (70.0%)
slight	6 (18.7%)	7 (25.0%)	9 (30.0%)
moderate	1 (3.1%)	0 (0.0%)	0 (0.0%)
marked	0 (0.0%)	0 (0.0%)	0 (0.0%)
Effect on salivation			
mouth dry	2 (6.3%)	4 (14.3%)	3 (10.0%)
mouth almost dry	16 (50.0%)	12 (42.9%)	12 (40.0%)
mouth moderately moist	14 (43.8%)	12 (42.9%)	15 (50.0%)
mouth moist	0 (0.0%)	0 (0.0%)	0 (0.0%)
Setting up of infusion			
easy	25 (78.1%)	24 (85.7%)	24 (80.0%)
fairly easy	3 (9.4%)	4 (14.3%)	5 (16.7%)
moderately difficult	4 (12.5%)	0 (0.0%)	1 (3.3%)
difficult	0 (0.0%)	0 (0.0%)	0 (0.0%)
Emetic effect			
none	32 (100.0%)	23 (82.1%)	29 (96.7%)
slight nausea	0 (0.0%)	3 (10.7%)	1 (3.3%)
severe nausea	0 (0.0%)	1 (3.6%)	0 (0.0%)
vomiting	0 (0.0%)	1 (3.6%)	0 (0.0%)

in the temazepam or midazolam groups ($p = 0.004$ and $p = 0.04$, respectively). There was no significant difference between residual sedation, apprehension, excitement, dizziness, effect on salivation, nausea, setting up of infusion or headache in the three groups (Kruskal–Wallis test). No adverse reactions were reported.

Discussion

The usefulness of different benzodiazepine derivatives as hypnotics the night before surgery was evaluated by our group[1,2] in many previous studies. Midazolam and temazepam have not as far as we know been compared. Both of them have been considered as effective in different kinds of transient insomnia.[5,9]

Our results show that oral temazepam 20 mg in a soft gelatin capsule guarantees a better sleep the night before surgery than does a placebo. Midazolam differed less significantly from placebo with respect to the hypnotic action. In our earlier studies midazolam has proved to be better than[7] or similar to[8] placebo as a hypnotic the night before surgery. Temazepam is clearly effective.[4] Both midazolam[3] and temazepam in a soft gelatin capsule[10] have a fast gastrointestinal rate of absorption especially in the upright position, and maximum blood levels and drug effect are reached about 30–45 minutes (t_{max}) after drug administration. There is, in supine subjects, as in premedication, a clearly slower rate of absorption and drug response, a t_{max} of 2 hours for midazolam[11] and 3 hours for temazepam.[4] There appears to be no significant difference between the two drugs studied. On the other hand, the quite slow distribution of temazepam[4,10] in comparison with the fast distribution and elimination[3,11] of midazolam, means that the effective levels of temazepam in the central pharmacokinetic compartment (including brain) last longer. This pharmacokinetic difference explains the somewhat better hypnotic effect of temazepam before operation.

In conclusion, the apparently longer lasting hypnotic and anxiolytic effect of temazepam makes it more useful than midazolam as a hypnotic before operation. However, in special cases, like nocturnal sedation before elective Caesarean section, midazolam has proved to be a good choice because there are practically no detectable levels of drug in the fetomaternal unit the next morning.[12]

References

1. Kanto J. The use of oral benzodiazepines as premedications: the usefulness of temazepam. *Acta Psychiatrica Scandinavica* 1986; **74** (Suppl. 332): 159–66.
2. Kanto J. Benzodiazepines as oral premedicants. *British Journal of Anaesthesia* 1981; **53:** 1179–88.
3. Allonen H, Ziegler G, Klotz U. Midazolam kinetics. *Clinical Pharmacology and Therapeutics* 1981; **30:** 653–61.
4. Salonen M, Aantaa E, Aaltonen L, Hovi-Viander M, Kanto J. A comparison of the soft gelatin capsule and tablet form of temazepam. *Acta Pharmacologica et Toxicologica* 1986; **58:** 49–54.
5. Kanto JH. Midazolam: the first water-soluble benzodiazepine pharmacology, pharmacokinetics and efficacy in insomnia and anesthesia. *Pharmacotherapy* 1985; **5:** 138–55.
6. Dundee JW, Moore J, Nicholl RM. Studies of drugs given before anaesthesia. I. A method of pre-operative assessment. *British Journal of Anaesthesia* 1962; **34:** 458–63.
7. Sjövall S, Kanto J, Kangas L, Pakkanen A. Comparison of midazolam and flunitrazepam for night sedation. A randomised double-blind study. *Anaesthesia* 1982; **37:** 924–8.
8. Sjövall S, Kanto J, Grönroos M, Himberg J-J, Kangas L, Viinamäki O. Antidiuretic hormone concentrations following midazolam premedication. *Anaesthesia* 1983; **38:** 1217–20.
9. Mitler MM. Evaluation of temazepam as a hypnotic. *Pharmacotherapy* 1981; **1:** 3–13.
10. Fuccella LM, Bolcioni G, Tamassia V, Ferrario L, Tognoni G. Human pharmacokinetics and bioavailability of temazepam administered in soft gelatin capsules. *European Journal of Clinical Pharmacology* 1977; **12:** 383–6.
11. Salonen M, Aantaa E, Aaltonen L, Kanto J. Importance of the interaction of midazolam and cimetidine. *Acta Pharmacologica et Toxicologica* 1986; **58:** 91–5.
12. Kanto J, Sjövall S, Erkkola R, Himberg J-J, Kangas, L. Placental transfer and maternal midazolam kinetics. *Clinical Pharmacology and Therapeutics* 1983; **33:** 786–91.

Anaesthesia, 1989, Volume 44, pages 688–689

Pain on injection of methohexitone

The use of lignocaine to modify pain on injection of methohexitone during anaesthesia for electroconvulsive therapy

K. H. Simpson, MB, ChB, FFARCS, Consultant, P. J. Halsall, MB, ChB, Clinical Assistant, C. A. Sides, MB, ChB, FFARCS, Senior Registrar, University Department of Anaesthesia, Clinical Sciences Building, St James's University Hospital, Leeds, LS9 7TF, J. F. Keeler, MB, BS, FFARCS, Registrar, Bradford Royal Infirmary, Bradford.

Summary

The present study was designed to assess the incidence of pain when methohexitone was administered to 35 depressed patients who had electroconvulsive therapy, and to determine whether the use of lignocaine could modify this, without affecting seizure duration. The same patients were studied during three separate treatment sessions; they received either methohexitone alone or mixed with, or preceded by, lignocaine 10 mg. Six (17%) patients spontaneously complained of pain during injection of methohexitone alone; the use of lignocaine prior to methohexitone reduced this to zero ($p < 0.05$). A total of 49% patients reported pain during injection of methohexitone; the use of lignocaine either mixed with, or given prior to, methohexitone significantly reduced this to 23% and 20% respectively ($p < 0.05$). Seizure duration was not significantly different during the three treatments.

Key words

Anaesthetics, intravenous; methohexitone.
Electroconvulsive therapy.

Methohexitone has been described as the drug of choice for anaesthesia for electroconvulsive therapy (ECT).[1,2] However, 40–60% patients experience pain during its injection into a vein on the dorsum of the hand prior to surgery,[3-5] but the incidence in patients who have anaesthesia for ECT is not known. Repeated anaesthesia is required for ECT treatment, and anticipation of pain on injection may be very distressing for patients, a pain which could be reduced if lignocaine is given with, or prior to, methohexitone.[5,6]

The present study was designed to determine the incidence of pain during injection of methohexitone prior to ECT treatment, and to assess whether it could be reduced by the use of lignocaine. A bilateral generalised convulsion must be produced during ECT if treatment is to be beneficial.[7] The use of lignocaine prior to ECT is usually avoided,[8] because it reduces seizure duration and renders treatment less effective.[9] The effect of lignocaine on seizure duration was therefore also recorded during the present study.

Methods

Thirty-five patients who had a course of bilateral ECT for treatment of depression were included in the study, which was approved by the Hospital Ethics Committee. Eight male and 27 female unpremedicated patients, aged 18–80 years and who weighed 43–90 kg, were studied. Patients gave informed verbal consent to participate, and none receiving treatment under the provisions of the Mental Health Act were involved.

Patients were studied during three consecutive ECT treatments over a period of 10–14 days, but not during the first treatment, because seizure duration is often prolonged at this time.[10] Concurrent medication was not altered during the study. Anaesthesia was induced with one of three regimens, the order of which was randomly selected for each patient. All subjects experienced all three methods of induction of anaesthesia on separate occasions.

Methohexitone only. Venepuncture was performed using a 23-gauge butterfly needle inserted into a small vein on the dorsum of the hand. One millilitre 0.9% saline was injected, and venous occlusion maintained for 60 seconds. Methohexitone was reconstituted with water to give a 10 mg/ml solution, and 9 ml of this was mixed with 1 ml 0.9% saline in a 10-ml syringe to produce 9 mg/ml methohexitone. Methohexitone 1 mg/kg was then injected over 60 seconds.

Methohexitone and lignocaine mixture as above and 0.9% saline 1 ml were injected; venous occlusion was maintained for 60 seconds. Methohexitone was reconstituted with water to give a 10 mg/ml solution, and 9 ml of this was mixed with 1 ml 1% lignocaine (10 mg) in a 10-ml syringe to produce 9 mg/ml methohexitone. Methohexitone 1 mg/kg was then injected over 60 seconds.

Lignocaine prior to methohexitone. The procedure was as above except that 1 ml 1% lignocaine (10 mg) was injected in place of saline. Methohexitone was reconstituted with water to give a 10 mg/ml solution, and 9 ml of this was mixed with 0.9% saline 1 ml in a 10-ml syringe to produce 9 mg/ml methohexitone. Methohexitone 1 mg/kg was then injected over 60 seconds.

The methohexitone was always freshly reconstituted using water at room temperature, and the lignocaine was preservative-free. The site of injection was varied so that a different vein was used each time, and only injections after 'clean' venepuncture were assessed.

The assessor was blind to the method of induction of

Accepted 23 August 1988.

anaesthesia. Spontaneous complaints of discomfort or pain were recorded as none, mild, moderate or severe during injection of methohexitone. Patients were then asked directly if the injection was comfortable; if it was not, they were asked if it was painful, and pain was graded as mild, moderate or severe. Each patient received 0.5 mg/kg suxamethonium, and their lungs were ventilated with 10 breaths of 100% oxygen using a Mapleson C system, after administration of methohexitone. A standard bilateral 3-second ECT stimulus was applied using an Ectron Duopulse machine, which delivered 33 J. Seizure duration was measured using the isolated forearm method.[11] Transcutaneous oxygen saturation was monitored during anaesthesia and during the seizure; the results of any patient whose $Sa\text{O}_2$ decreased to less than 90% were excluded.

Data were analysed using one-way analysis of variance, the Kruskall–Wallis analysis of variance, the Mann–Whitney *U* test and the Chi-squared test where appropriate.

Results

Six patients (17%) spontaneously complained of pain (two mild, one moderate and three severe) when methohexitone was administreed without lignocaine. Two patients (6%) spontaneously reported pain (one mild and one moderate) when methohexitone was mixed with lignocaine; this reduction was not significant. There were no spontaneous complaints of pain when lignocaine was given prior to methohexitone which was significant ($p < 0.05$).

More reported pain on injection when they were questioned directly than had complained spontaneously ($p < 0.05$). A total of 17 (49%) patients experienced pain (seven mild, six moderate and four severe) when methohexitone was administered without lignocaine. Eight patients (23%) complained of pain (six mild and two moderate) when lignocaine was mixed with methohexitone. Seven patients (20%) reported pain (six mild and one moderate) when lignocaine was given before the methohexitone. The use of lignocaine either mixed with, or given before, methohexitone significantly reduced the incidence of pain on injection when compared with methohexitone alone ($p < 0.05$).

There was no significant difference between the groups in mean (SD) seizure duration: methohexitone alone 29.1 (9.32) seconds, lignocaine mixed with methohexitone 28.4 (11.8) seconds, and lignocaine prior to methohexitone 29.3 (13.4) seconds.

Discussion

Patients who have anaesthesia for ECT form a unique group, since they usually require several anaesthetics during a period of a few weeks, which allows the anaesthetist the opportunity to provide an optimum anaesthetic for each patient.[12] The present study has shown that during anaesthesia for ECT, pain on injection of methohexitone into a vein on the dorsum of the hand occurred in 49% patients, and in approximately half of these subjects, pain was moderate or severe. Only 17% patients complained spontaneously of pain, but a further 32% reported pain when asked directly. Patients who have ECT are often fearful and withdrawn, and many expect a certain amount of discomfort to be associated with the procedure, and may therefore not complain spontaneously.

It is possible to reduce the incidence of pain on injection by using a large vein in the antecubital fossa,[13] but this has the disadvantage that intravenous access may be lost during the ECT seizure. The present study has shown that the administration of 10 mg lignocaine (1%) prior to methohexitone significantly reduces pain on injection, both volunteered spontaneously and detected by questioning, without adversely affecting seizure duration during ECT treatment. Pain during injection is often perceived as a trivial problem, but may be a source of anxiety for patients.[14] Lignocaine should be used routinely when injecting methohexitone into a vein on the dorsum of the hand; this is particularly important when repeated anaesthesia is planned.

References

1. Allen RE, Pitts FN Jr, Summers WK. Drug modification of ECT: methohexital and diazepam. II. *Biological Psychiatry* 1980; **15:** 257–64.
2. Woodruff RA Jr, Pitts FN Jr, McClure JN Jr. The drug modification of ECT. 1. Methohexital, thiopental, and preoxygenation. *Archives of General Psychiatry* 1968; **18:** 605–11.
3. Goold JE. Pain after the injection of methohexitone. *Anaesthesia* 1982; **37:** 213.
4. Collins KM, Willatts, DG, Goulding CA. Pain after injection of methohexitone. *Anaesthesia* 1983; **38:** 1002.
5. Millar JM, Barr AM. The prevention of pain on injection. A study of the effect of intravenous lignocaine before methohexitone. *Anaesthesia* 1981; **36:** 878–80.
6. Heath PJ, Pearce AJ, Hankova M, Bastiaenen HLR. Pain-free intravenous injections. *Anaesthesia* 1988; **43:** 65.
7. Fink M. *Convulsive Therapy: theory and practice.* New York: Raven Press, 1979.
8. Rouse EC. Propofol for electroconvulsive therapy. A comparison with methohexitone. Preliminary report. *Anaesthesia* 1988; **43** (Suppl.): 61–4.
9. Cronholm B, Ottosson JO. Experimental studies of the therapeutic action of electroconvulsive therapy in endogenous depression. *Acta Psychiatrica et Neurologica Scandanavica* 1960; **35** (Suppl. 145): 69–101.
10. Maletzky BM. Seizure duration and clinical effect in electroconvulsive therapy. *Comprehensive Psychiatry* 1978; **19:** 541–50.
11. Fink J. Johnson L. Monitoring the duration of electroconvulsive therapy seizures. *Archives of General Psychiatry* 1982; **39:** 1189–91.
12. Rich CL, Smith NT. Anaesthesia for electroconvulsive therapy; a psychiatric viewpoint. *Canadian Anaesthetists' Society Journal* 1981; **28:** 153–7.
13. McCollum JSC, Dundee JW. Comparison of induction characteristics of four intravenous anaesthetic agents. *Anaesthesia* 1986; **41:** 995–1000.
14. Rowlands DE. Pain after methohexitone. *Anaesthesia* 1969; **24:** 289.

Anaesthesia, 1989, Volume 44, pages 690–706

Correspondence

Clinical freedom: better and best 690
R.R. Macmillan, FFARCS
Anaesthetists, lawyers and the public 691
J.E. Utting, JP, FFARCS
Treatment of epidural morphine-induced pruritus with buprenorphine 691
J.P. Keaveny, FFARCS and N.J.N. Harper, FFARCS
A complication of povidone–iodine 692
P. Joshi, FFARCS
Weight determined dosage of vecuronium bromide 692
M.J. Harrison, FFARCS and K. Gunn, MB, ChB
A capnographic caution 693
A. Yates, FFARCS and J. M. Eaton, FFARCS
L. Marshall and G.D. Lowe 693
Acrylic cement in hip surgery 694
M.L. James, FCAnaes
J.A.T. Duncan, FFARCS 695
A postoperative neurological problem 695
A. Kitching, MB, ChB, BSc and S. Taylor, FFARCS
Headache after dural puncture 696
P. Barker, FCAnaes
H. Flaatten, MD 696
Propofol and fentanyl anaesthesia 697
K.M. Sherry, FFARCS, N.J.A. Massey, FFARCS and C.S. Reilly, FFARCS
G.N. Russell, FFARCS 697
The choice of anaesthesia for the very old 697
M. Lim, FFARCS, MRCP, D.N. Campbell, FFARCS and R. Morris, MSc
M.P. Hosking, MD, C.M. Lobdell, MD, M.A. Warner, MD, K.P. Offord, MS and L.J. Melton, MD 698
Asystole on induction 698
K. Ruiz, B Med Sci, MB, ChB
Anaesthesia in myotonia dystrophica 699
B.J. Pollard, B. Pharm, FFARCS and T.M. Young, FFARCS
Failure of Heimlich manoeuvre 699
P. Sagar, MB, BS amd J.S. Goodman, MB, ChB
A 10-second convulsion during propofol injection? 700
I.H. Herrema, FFARCS
Costs of replacement of anaesthetic equipment 700
E. Moss, MD, FFARCS
Keeping the position of the 29-gauge spinal needle 707
M.E. Tunstall, FFARCS, D Obst RCOG
Debris in a breathing system 702
B.L. Taylor, BSc, FFARCS, C. Rainbow, SRN and D. Ford
L. Marshall and G.D. Lowe 702
Large tonsils and the laryngeal mask airway 703
P.V. van Heerden, FFARCSI and D. Kirrage, MB, ChB, MRCGP
Chain of errors 703
R.W. Okell, MRCP, FFARCS
Embolectomy without bypass 704
P.T. Sotunmbi, DA, FMCA, S.D. Amanor-Boadu, DA, FMCA and A.A. Sanusi, MB, BS
Unusual cause of obstructed expiration 704
P. Johnston, FFARCS
The oesophageal detector device 705
I. Calder, DRCOG, FFARCS, M. Smith, FFARCS and M. Newton, FFARCS
The use of a transparent mouthguard at induction 705
G. Beneby, FFARCS
Another use of the pulse oximeter 705
E.V. Pillai, FFARCSI and S.K. Thas, FFARCS
'Talking in their sleep'—a defensive practice 706
G.D. Stanley, MB, ChB, DA
Subarachnoid anaesthesia with 0.25% isotonic bupivacaine for Caesarean section 706
A.J. Wilson, MB, ChB, DA

Clinical freedom: better and best

The letter about clinical freedom from Professor Healy cannot pass without comment. Medicine is a more exact science in 1989; however, I do not agree that there are studies which show that particular strategies provide the best management of many diseases or choice of techniques in surgical and anaesthetic practice. Many studies show a technique to be statistically no different or better than another in some respects; this is very different from the best, which, by definition, must be better in every respect. The fallacy of the author's statement is apparent when he is obliged to use the phrase 'in my opinion' about the best technique for laparoscopy. If a technique was clearly the best then undoubtedly all would use it. I, incidentally, intubate my patients' tracheas for laparoscopy but cannot categorically state that others must do likewise.

The argument that anaesthetists are denied the appropriate instruments by a third party, the Health Authority, is a popular one. Nevertheless, without infinite resources one person's oximeter is another person's fetal heart monitor. We, the clinicians, should have the ability to determine priority when equipment is bought, and certainly this is not an uncommon situation. Is there any evidence of a difference in immediate peri-operative mortality between countries that monitor very extensively and those that do not? The publication of suggested standards for monitoring should have a scientific basis if we are to claim that

---

*All correspondence should be addressed to Dr J. N. Lunn, Editor of *Anaesthesia*, Department of Anaesthetics, University Hospital of Wales, Heath Park, Cardiff CF4 4XW, United Kingdom.

Letters must be typewritten on one side of the paper only and double spaced with wide margins. Copy should be prepared in the usual style and format of the Correspondence section. Authors must follow the advice about references and other matters contained in the Notice to Contributors to *Anaesthesia* printed at the back of each issue. The degrees and diplomas of each author must be given in a covering letter personally signed by all the authors.

Correspondence presented in any other style or format may be the subject of considerable delay and may be returned to the author for revision. *If the letter comments on a published article in Anaesthesia, please send three copies; otherwise two copies of your letter will suffice.*

medicine is now more scientific. The recent recommendations from the Association acknowledge that there is no conclusive evidence of a reduction in mortality or morbidity and are based therefore more on commonsense than science.

The Colleges, Faculties and Associations have failed to arrange nationally based schemes to examine practice and determine what is 'the best' without the need for the qualifying 'in my opinion'. The CEPOD report and its companion on maternal mortality are the nearest, but they have yet to tell me the best way to conduct a laparoscopy. Let us not confuse stupidity and arrogance with commonsense and clinical freedom, or believe that there is an unlimited source of funding to procure all for all.

3 Albany Avenue,
Eccleston Park,
Prescot L34 2QN
R.R. MACMILLAN

Anaesthetists, lawyers and the public

Your courageous editorial on this subject (*Anaesthesia* 1989; **44:** 1) contains, despite its virtues, much which is naive. Your idea, to provide medicolegal articles by a lawyer is an excellent one, but you do ill to compare medicine and the law to the detriment of the former. Fifteen years of sitting in courts of Petty Jurisdiction, where the greater part of criminal work is dealt with, and a longer period occasionally giving 'expert' advice to plaintiffs, have convinced me that professional competence, expertise and dedication are of a higher order among doctors than lawyers. The Law Society has a very long fuse. Settlements for plaintiffs may, or may not, be 'mean', as you suggest, but legal fees certainly are not. There is no need for feelings of inferiority.

You appear to believe that public punishment should follow a medical catastrophe in which the doctor has been culpable. This would not, however, bring a patient back to life or restore his wits. It would certainly be unlikely to increase public confidence. But a sense of injustice sometimes remains. Some years ago, after a local enquiry into an accident in which the anaesthetist had been culpable, a Chairman of a Health Authority (not in Liverpool) remarked that he had just confirmed the sacking of a porter for stealing two pound coins, but that in this case the anaesthetist would get off without so much as a warning. This was an over-simplification, but he had a point. Nevertheless, the mechanisms for punishment do exist and perhaps they should be used more often.

A more positive approach would be for us to be less inhibited about criticising our colleagues when it is realised that their conduct is falling below the acceptable. Audit, to which you have personally paid a most distinguished contribution, should go some way in this respect. A new method of punishment probably would not. In the meanwhile, as Wylie pointed out 'There but for the grace of God . . .'.

Royal Liverpool Hospital,
PO Box 147,
Liverpool L69 3BX
J.E. UTTING

Treatment of epidural morphine-induced pruritus with buprenorphine

A 44-year-old man was admitted to the Casualty Department after a road traffic accident. He was fully conscious and complained of right-sided chest pain. He was centrally cyanosed and tachypnoeic. Surgical emphysema, a flail segment of ribs 4–10 and a clinical pneumothorax were noted and confirmed radiologically. Blood gases were pH 7.39, $P\text{aO}_2$ 8.7 kPa, $P\text{aCO}_2$ 4.4 kPa, breathing air. Fifty percent oxygen was administered via Venturimask; a chest drain was inserted and connected to an underwater seal and the patient was transferred to ITU.

A thoracic epidural was inserted at T_{7-8} and a continuous infusion of bupivacaine 0.125% with adrenaline 1:400000 with preservative-free morphine 2 mg in 50 ml was started at 2–4 ml/hour. This provided excellent analgesia and caused marked clinical improvement. Twenty-four hours later the patient complained of severe, unremitting pruritus over the face, arms and upper trunk. This was not relieved by intravenous chlorpheniramine 10 mg. The epidural infusion was discontinued and replaced by bupivacaine 0.125% with adrenaline 1:400000 with buprenorphine 0.6 mg to a volume of 50 ml infused at a similar rate. This also resulted in excellent analgesia and the patient sustained rapid and complete relief from pruritus. This infusion was continued for 10 days and pruritus did not recur.

The epidural morphine was replaced by epidural buprenorphine in an attempt to provide adequate analgesia without pruritus. It is well known that pain and pruritus are closely related.[1,2] Intravenous and epidural opioids may produce pruritus which is reversed by intravenous naloxone. Studies which involved epidural buprenorphine describe a very low incidence of pruritus.[3] Buprenorphine is a partial agonist–antagonist of the morphine type and is used as an antagonist after intravenous fentanyl anaesthesia. It is an effective analgesic with few minor side effects, and a partial Mu-agonist, more lipophilic than morphine, which suggests that it may be more appropriate for epidural use, has a high opiate receptor occupancy rate and is known to dissociate slowly from its receptor site. It appears to provide very effective postoperative analgesia without pruritus when given by the epidural route.

Manchester Royal Infirmary,
Oxford Road,
Manchester M13 9WL
J.P. KEAVENY
N.J.N. HARPER

References

1. GUSTAFSSON LL, SCHILDT B, JACOBSEN K. Adverse effects of extradural and intrathecal opiates: report of a nationwide survey in Sweden. *British Journal of Anaesthesia* 1982; **54:** 479–86.
2. JAFFE JH, MARTINS WR. Narcotic analgesics. In: GOODMAN LS, GILMAN A, eds. *The pharmacological basis of therapeutics*, 5th edn. New York: Macmillan, 1970.
3. LANZ E, SIMCO G, THEISS D, GLOCKE M. Epidural buprenorphine—a double-blind study of postoperative analgesia and side effects. *Anesthesia and Analgesia* 1984; **63:** 593–8.

A complication of povidone–iodine

Tachyarrhythmias caused by povidone–iodine during intra-abdominal irrigation to treat sepsis are not described: this is a report of a case.

A 79-year-old woman presented with an acutely painful abdomen and required surgery. The pre-operative visit revealed a history of atrial fibrillation controlled with 0.0625 mg digoxin. An arterial blood pressure of 140/80 mmHg was recorded and her ECG showed sinus rhythm with a rate of 100 beats/minute. No premedication was given; anaesthesia was commenced after a rapid sequence induction using etomidate 12 mg, suxamethonium 60 mg and maintained with isoflurane 1%, oxygen and nitrous oxide. Vecuronium (9 mg) and fentanyl (0.3 mg) were given in addition, to provide muscle relaxation and analgesia. Intra-operatively the following variables were monitored continuously: arterial blood pressure, electrocardiogram, end-tidal carbon dioxide, central venous pressure, train-of-four and pulse oximetery, and the patient was observed for signs of sympathetic overactivity.

Her arterial blood pressure remained stable at approximately 160/90 mmHg; her pulse rate was 100 beats/minute in sinus rhythm, and muscle relaxation was judged to be adequate using a peripheral nerve stimulator. However, after an abdominal washout with a lukewarm diluted solution of povidone–iodine started, for rupture of an empyema of her gall bladder, the pulse rate immediately increased from 100 beats/minute in sinus rhythm to 160 beats/minute, and the ECG showed atrail fibrillation, but there were no changes in the other measured variables.

Attempts were made to reduce the heart rate with carotid sinus massage, and then incremental verapamil (5 mg). The serum potassium was 3.4 mmol/litre and 40 mmol of potassium were given. These mechanical and therapeutic manoeuvres were without success. No further complications occurred during the course of the operation. The patient was given digoxin 0.125 mg intravenously after completion of the anaesthetic. This reduced the heart rate to 120 beats/minute. The patient's progress after operation was uneventful. Her heart rate returned to 80 beats/minute, but was still irregular despite normal serum potassium levels and therapeutic digoxin levels.

No toxic effects were observed after the single use of intraperitoneal povidone–iodine.[1] It is nonirritant[2] and is unlikely to cause iodine sensitisation.[3] Povidone (polyvinylpyrrolidone) is used as a carrier substance, with the additional property of a reduction of the irritant effects of iodine and was formerly introduced as a plasma expander. It has not in the past exhibited any arrhythmogenic properties. Iodine is a well proven antiseptic which may appear in the serum after its use intraperitoneally[1] and may depress thyroid function after operation.[4] Acute tachycardia has not been reported before. In conclusion, it is difficult to explain the mechanism of this tachyarrhythmia; however, one should beware of such problems in those groups of patients at risk from cardiovascular complications, especially in view of the fact that there is no product licence for body cavity irrigation with povidone–iodine.

St George's Hospital,
London SW17
P. Joshi

References

1. Sindelar WF, Mason GR. Intraperitoneal irrigation with povidone–iodine solution for the prevention of intra-abdominal abscesses in the bacterially contaminated abdomen. *Surgery, Gynecology and Obstetrics* 1979; **148:** 409–11.
2. Gupta HC, Maurya SD, Sharma BD, Argawal RK. Intraperitoneal irrigation with betadine (povidone–iodine) solution in management of patients with diffuse peritonitis. *The Clinician* 1986; **50:** 118–23.
3. Kothuis BJL. The effect of povidone–iodine on postoperative wound infection in abdominal surgery. *The Netherlands Journal of Surgery* 1981; **33:** 186–9.
4. Weissenhofer W. Effects of betadine solution on bacterial peritonitis. In: Altemeier WA, ed. *World congress/antisepsis: the proceedings.* New York: H.P. Publishing Co., Inc., 1980: 72–4.

Weight determined dosage of vecuronium bromide

The use of gross body weight to determine the dosage of drugs is ubiquitous. We wish to report some serendipitous observations. We noticed, during a study of infusions of vecuronium bromide in a group of 30 patients who had prolonged surgery, that after the induction dose of vecuronium (0.1 mg/kg) the heavier patients took longer to recover.

The effect of the neuromuscular blocker was measured with a Datex Relaxograph. Anaesthesia was induced with thiopentone, and maintained with nitrous oxide and oxygen (2:1), isoflurane 0.5% and fentanyl. The end-point, at which the duration of action of the drug was noted, was when the height of the first twitch of the train-of-four was 10% of control.

There were nine patients who weighed 45–64 kg; the mean duration of action of 0.1 mg/kg vecuronium was 24 (SD 8) minutes. There were eight patients who weighed 80–99 kg; in these patients the duration of vecuronium was 37 (SD 8) minutes. Using the Student's *t*-test this is a significant difference, $p < 0.005$.

The Auckland University Department of Surgery measures fat-free mass (FFM) using *in vivo* neutron activation and, on request, supplied us with a 'rule-of-thumb' guide to determination of FFM.

$$\text{FFM (kg)} = [\text{Gross weight (kg)} \times 0.65] + 6.5$$

We anaesthetised 30 subsequent patients, and used 0.1 mg/kg FFM of vecuronium. There were 10 patients using the same technique as described above whose gross weight was in the 45–64 kg group; the duration of vecuronium 0.1 mg/kg was 21 (SD 8) minutes. Eleven patients weighed 80–99 kg; the duration of action of vecuronium in these patients was 21 (SD 6) minutes. These groups of patients were not significantly different (Student's *t*-test). The ages of the patients in the two groups were slightly different, 55 (SD 20) years and 41 (SD 17) years, the weights were 66 (SD 20) kg and 72 (SD 16) kg, respectively.

It is obvious on reflection that the prolonged action of vecuronium in the heavy patients should be so, since muscle relaxants are almost insoluble in fat.[1] This may have little impact in clinical practice, but in academic work should not doses of muscle relaxants be determined by the fat-free mass and not gross body weight?

Auckland Hospital,
Auckland 1,
New Zealand
M.J. Harrison
K. Gunn

Reference

1. Cohen EN, Hood N, Golling R. Use of whole-body autoradiography for determination of uptake and distribution of labeled muscle relaxants in the rat. *Anesthesiology* 1968; **29:** 987–93.

A capnographic caution

We wish to report a source of possible confusion in the use of capnography in conjunction with the Pall Ultipor Breathing System Filter, resulting in erroneously high expired carbon dioxide readings.

A fit 53-year-old woman with normal lung function was anaesthetised for a right pneumonectomy. She was intubated with a medium-sized left Robertshaw tube and placed in the left lateral position, at which stage the tube was checked for proper placement and function. Ventilation of the lungs was provided with a Penlon Nuffield 400 via a circle with an Ohmeda Mk 4A absorber. The fresh gas flow was about 6 litres/minute. Blood pressure, electrocardiogram, airway pressure and inspired/expired carbon dioxide were all monitored; the latter was sampled at a flow rate of 1.5 litres/minute between the circle and the catheter mount via a T-piece (see Fig. 1), using a Datex CD 101 analyser, and the sample was not returned to the circle system.

All variables were stable and the operation commenced. A Pall Ultipor Filter was inserted at this stage into the system between the circle and the capnograph T-piece (Fig. 1, position A). The end-expired CO_2 was noted to increase almost immediately from 4.8 to 6.0% and the inspired CO_2 from 0.4 to 2.0%. All other variables were stable and the chest wall was not opened, so introduction of the filter was suspected as the cause. The readings decreased to their previous values when it was removed from the system.

The filter was reintroduced at three other positions; on the outflow and inflow connexion to the absorber, and between the catheter mount and the T-piece (Fig. 1, positions B, C, and D). None of these positions caused a change in the readings, but with the filter back in its original position, elevated levels of end-tidal CO_2 were again displayed. The T-piece sampling limb was clamped, with the filter left in this position, and a reading of end-tidal CO_2 was taken via a needle inserted into the catheter mount close to the tube. Normal readings of end-tidal CO_2 were acquired, and proved that the elevated readings obtained previously were spurious. All of the above was performed prior to the chest wall being opened and when the other measured variables were stable.

We have reproduced these findings to a greater or lesser degree in subsequent cases with new filters on each occasion and with the same analyser and similar breathing systems.

The instructions issued with the Pall Ultipor filter give clear directions for the possible locations within systems,[1] including the position used in this case. The user is cautioned to evaluate the effect of mechanical dead space individually for each patient. It is stated that compensation may be necessary as indicated by clinical assessment, arterial blood gas analysis or end-tidal gas measurements. The literature on this and other filters, although dealing with humidification[2-4] and bacterial filtration,[4,5] contains little information on the physical properties.[4,6,7] No article reports our findings.

It is our view that placement of the capnographic sampling head in relation to a filter is important, and, in the wrong position, may cause erroneous readings to be displayed. This may result in unnecessary alterations in ventilator settings, which could in itself be deleterious to the wellbeing of the patient. Ideally, all respiratory monitoring should be as close to the tracheal tube as possible, but this in itself caused problems. We hope, in the absence of an adequate explanation, that this letter will at least serve as a warning that care is necessary when filters are used with CO_2 sampling from anaesthetic systems.

Frenchlay Hospital, A. YATES
Bristol BS16 1LE J.M. EATON

References

1. Pall Ultipor Breathing System Filter. Instructions for use. Pall Biomedical Ltd, Europa House, Havant Street, Portsmouth PO1 3DP.
2. CHALON J, MARKHAM JP, ALI MM, RAMANATHAN S, TURNDORF H. The pall ultipor breathing circuit filter—an efficient heat and moisture exchanger. *Anesthesia and Analgesia* 1984; **63:** 566–70.
3. PRIMIANO FP, MORANZ ME, MONTAGUE FW, MILLER RB, SACHS DPL. Conditioning of inspired air by a hygroscopic condenser humidifier. *Critical Care Medicine* 1984; **12:** 675–8.
4. SHELLY M, BETHUNE DW, LATIMER RD. A comparison of five heat and moisture exchangers. *Anaesthesia* 1986; **41:** 527–32.
5. GALLAGHER J, STRANGEWAYS JEM, ALLT-GRAHAM J. Contamination control in long-term ventilation. A clinical study using a heat- and moisture-exchanging filter. *Anaesthesia* 1987; **42:** 476–81.
6. SCHENA J, THOMPSON J, CRONE RK. Mechanical influences on the capnogram. *Critical Care Medicine* 1984; **12:** 672–4.
7. BUCKLEY PM. Increase in resistance of inline breathing filters in humidified air. *British Journal of Anaesthesia* 1984; **56:** 637–43.

A reply

The use of capnographic monitoring equipment provides valuable information to the anaesthetist and the use of such equipment in conjunction with a heat and moisture exchanging filter, HMEF, (Pall Ultipor) has become increasingly widespread. The findings of Drs Eaton and Yates do serve to highlight that it is quite possible to obtain correct end-expiratory CO_2 readings when a filter is used in combination with capnographic equipment. This is the case when the filter is positioned for either of the recommended modes of use i.e. as an inspiratory/expiratory filter or as an HMEF.

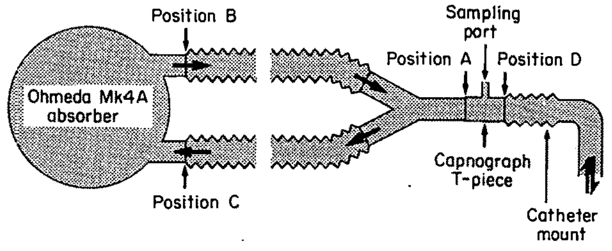


Fig. 1.

Their observations may well be due to the modifying effects that a heat and moisture exchanger (HME) has on the patient side environment and could be true for HMEs other than Pall.

When an HME is placed between the Y-piece and the patient tube, its action changes the physical nature of the environment on either side. What is of interest in this case is the changes on the patient side of the device, around the capnograph port, which resulted in the unusual readings.

Several physical changes occur including increased humidity, temperature variation, gas flow patterns, volume changes and the presence of small amounts of condensed water. Any of these factors may be implicated in the change in CO_2 as measured by Drs Eaton and Yates. Furthermore, one cannot discount the effect of these changes on the gas sampling efficiency of the capnograph T-piece or possible interference with the capnograph transducer itself.

We believe that this observation requires extensive testing and intend to investigate all variables fully to establish the cause of these unexplained readings. Such an analysis would be of interest to all using HMEs in anaesthetic systems. However, the normal readings obtained when expired gases were sampled by needle from the catheter, only serve to make understanding of the nature of the unexplained readings less easy.

We suggest in the meantime that placing the capnograph port distal to the Pall filter would serve not only to prevent the recurrence of such readings, but would also protect the T-piece and capnograph from microbial contamination.[1,2] We also emphasise that, with the exception of the authors' readings at position A, their general observations confirm the findings of other workers. Previous studies have demonstrated that when the Pall Ultipor Breathing System Filter is used as an HME in a variety of breathing systems, there are no significant changes in either arterial CO_2 tension or end-expiratory CO_2 levels.[3-5]

We thank Drs Eaton and Yates for drawing this important aspect of filter use to our attention. We intend further investigation to establish the cause of this spurious reading.

Pall Biomedical Ltd
Portsmouth,
Hants PO1 3PD

L. MARSHALL
G.D. LOWE

References

1. NICHOLL ADJ, LATIMER RD, BETHUNE DW. The humidification, bacterial and viral filtration in anaesthesia and intensive care. Proceedings of the European Association of Cardiothoracic Anaethesiologists, 19–21 May 1988, Gottingen.
2. GALLAGHER J, STRANGEWAYS JEM, ALLT-GRAHAM J. Contamination control in long-term ventilation. A clinical study using a heat and moisture exchanging filter. *Anaesthesia* 1987; **42:** 476–81.
3. CHALON J, MARKHAM JP, ALI MM, RAMANATHAN S, TURNDORF H. The Pall Ultipor breathing circuit filter. An efficient heat and moisture exchanger. *Anesthesia and Analgesia* 1984; **63:** 566–70.
4. ROMANO E, GULLO A, VACRI A, BONIFACIO R, CARISTI D. Effects of a heat and moisture exchanger on carbon dioxide equilibrium during mechanical ventilation with the Bain circuit. *European Journal of Anaesthesiology* 1987; **4:** 183–6.
5. MERRILL SB. Pall heat and moisture exchanger filter. Effect on end tidal CO_2 values. Personal communication.

Acrylic cement in hip surgery

The article by Dr Duncan (*Anaesthesia* 1989; **44:** 149–53) raises a question that has been discussed for many years. To what extent is bone cement (methyl methacrylate), and in particular the monomer, responsible for the cardiovascular collapse sometimes seen when joint protheses are inserted?

The dose of monomer required to be injected into dogs to produce hypotension is possibly 35 times higher than that amount calculated to be released in man during hip arthroplasty.[1] When Modig injected monomer into dogs to achieve levels that occur in man during arthroplasty, no changes in haematological or cardiopulmonary variables were found.[2] No correlation was found during total hip arthroplasty in man between levels of methyl methacrylate and its first metabolite methacrylic acid and blood pressure.[3] It is unlikely therefore that monomer is the cause.

Inert substances inserted under pressure into the femur do cause cardiopulmonary changes. Pelling and Butterworth compared plasticine, soft paraffin wax and acrylic cement in cats and rabbits.[4] They found similar effects on blood pressure, central venous pressure and pattern of respiration with each substance when it was forcibly inserted into unwashed femoral canals. Bone cement was no worse than the other materials.

These changes can be minimised or abolished by the use of a high pressure jet of saline to wash out the femoral canal[5] and retrograde insertion of the cement. It is possible that effective washout reduces the amount of bone marrow contents and especially fat (in which monomer is very soluble) that could be released into the circulation during cementation.

There are undoubted long-term benefits from cementing the prothesis in place. Survival by 84 days was better in Duncan's series for the cemented group (87%) compared to the noncemented (74%). It therefore seems wise to use such a technique, despite the fact that the one-month mortality is worse.

A further reduction in morbidity can be achieved by retrograde filling of the femur with the Exeter cement gun. This was designed[6] to improve fixation by avoiding air pockets that occur when cement is implanted by hand, and to lessen the risk of such air being forced into the circulation. There is no need for the use of holes in the side of the femur, and indeed such holes lessen the efficacy of fixation of the prothesis.

There was no difference in a series reported from Exeter in 1971[7] in the one-month mortality after cemented Thompson and uncemented Austin–Moore protheses, although the rates were higher in those days (16% and 17% respectively) when retrograde filling was not fully developed. The Thompson operation gave a much better functional result as well.

In view of these observations it is prudent to adopt three measures that seem to reduce untoward cardiopulmonary events.

There is no doubt that correct fluid balance in this procedure is essential. These elderly patients, who have surgery for fractured neck of the femur, face a second episode of trauma with further disturbance of their already deranged fluid balance. Antiplatelet drugs are almost always used prior to elective arthroplasty to reduce venous thrombosis and embolism. High pressure jet saline washout of the prepared bone surface and retrograde filling help to reduce these complications. Moreover they enable much better fixation of the cement in the bone matrix to be achieved.

Royal Devon and Exeter Hospital,
Exeter EX2 5DW

M.L. JAMES

References

1. McLaughlin RE, DiFazio CA, Hakala M, Abbott B, MacPhail JA, Mack WP, Sweet DE. Blood clearance and acute pulmonary toxicity of methlmethacrylate in dogs after simulated arthroplasty and intravenous injection. *Journal of Bone and Joint Surgery* 1973; **55-A:** 1621–9.
2. Modig J, Busch C, Waernbaum G. Effects of graded infusions of monomethylmethacrylate on coagulation, blood lipids, respiration and circulation. An experimental study in dogs. *Clinical Orthopaedics and Related Research* 1975; **113:** 187–97.
3. Crout DHG, Corkill JA, James ML, Ling RSM. Methylmethacrylate metabolism in man. The hydrolysis of methacrylate to metacrylic acid during total hip replacement. *Clinical Orthopaedics and Related Research* 1979; **141:** 90–5.
4. Pelling D, Butterworth KR. Cardiovascular effects of acrylic bone cement in rabbits and cats. *British Medical Journal* 1973; **2:** 638–41.
5. Sherman RMP, Byrick RJ, Kay JC, Sullivan TR, Waddell JP. The role of lavage in preventing hemodynamic and blood-gas changes during cemented arthroplasty. *Journal of Bone and Joint Surgery* 1983; **65-A:** 500–6.
6. Evans RD, Palazzo MGA, Ackers JWL. Air embolism during total hip replacement: comparison of two surgical techniques. *British Journal of Anaesthesia* 1989; **62:** 243–7.
7. Wrighton JD, Woodyard JE. Prosthetic replacement for subcapital fractures of the femur: a comparative survey. *Injury* 1971; **2:** 287–93.

A reply

Dr James puts his finger on the nub of the matter. Polymethyl methacrylate cement has been associated for many years with intra-operative collapse, but no direct link between this and the acrylic monomer has emerged. The cardiopulmonary changes may indeed be reproduced by forcible insertion of inert substances into unwashed femoral canals.

My orthopaedic colleagues have, for some years now, incorporated into their routine practice all the refinements of hip surgery technique developed in Exeter. Despite this, the anaesthetist in charge of a healthy patient undergoing elective total hip replacement will repeatedly have occasion to confirm Modig's observations[1] of a transient decrease both in arterial blood pressure and arterial oxygen saturation, shortly after the insertion into the femoral canal of the bone cement. The Exeter refinements, while useful, do not, therefore, of themselves explain or prevent the cardiopulmonary changes. They do, however, make the elective operation safer.

The situation is less satisfactory in the case of metal prostheses grouted in bone cement after subcapital fracture of the neck of femur. My colleagues and I find it difficult to accept the purely statistical justification of the high intra-operative mortality thereto attaching. Dr James is right to stress the importance of preparing these trauma patients fully, with especial attention to fluid balance, antiplatelet drugs, and the details of the technique employed. One is still left, even after due consideration of these factors, with the uncomfortable fact of an operative mortality of 7–22%[2] from a process that can be neither controlled nor explained.

It is the purpose of clinical audit to make such decisions in the light of balanced argument with carefully weighed facts.

West Fife Hospital,
Dunfermline KY12 7EZ
J.A.T. Duncan

References

1. Modig J, Malmberg P. Pulmonary and circulatory reactions during total hip replacement surgery. *Acta Anaesthiologica Scandinavica* 1975; **19:** 219–37.
2. Gresham GA, Kuczynski A, Rosborough D. Fatal fat embolism following replacement arthroplasty for transcervical fractures of femur. *British Medical Journal* 1971; **ii:** 617–9.

A postoperative neurological problem

We wish to report a case of postoperative paraplegia which occurred in a patient who received general anaesthesia without regional anaesthesia of any kind. We believe it is very important that such cases are reported since neurological lesions that occur postoperatively are blamed so often on local anaesthetic techniques.

A 73-year-old female presented for routine cholecystectomy. She had no significant medical problems other than obesity and her only regular medication was a laxative. She received several uneventful general anaesthetics previously for treatment of a transitional cell bladder tumour; the last one was in 1984.

Premedication was with diazepam 10 mg orally 2 hours before operation and she received prophylactic heparin, 5 000 units, subcutaneously. ECG and noninvasive blood pressure monitoring was commenced in the anaesthetic room. Anaesthesia was induced with thiopentone 225 mg, and tracheal intubation was easily achieved after pancuronium 6 mg. Anaesthesia was maintained with nitrous oxide, oxygen, halothane and morphine. She received one litre of compound sodium lactate solution during the operation. Intra-operative monitoring consisted of ECG, noninvasive blood pressure, end-expired carbon dioxide, fractional inspired oxygen concentration and airway pressure. Her blood pressure and heart rate were stable throughout surgery, which lasted one hour and 10 minutes and was uneventful.

Her postoperative progress was also uneventful until the third postoperative day, when she suddenly developed severe pain at the L_{3-4} lumbar level. Her right leg became completely flaccid and she developed sensory loss in her left leg. She was unable to pass urine and required bladder catheterisation.

Physical examination revealed complete paralysis of the right leg with parasthesiae in the dermatomal distribution of L_3 bilaterally, and loss of sensation to pinprick in the dermatomal distribution of L_{4-5} and S_1 on the left side. Tendon reflexes were equivocal, but both plantar reflexes were extensor. A myelogram performed the same evening showed no lesion, and a CT scan excluded extrinsic cord compression, but the spinal cord appeared oedematous, possibly secondary to an infarction of the cord.

Sensation had virtually returned to normal after 2 days, but the weakness of her right leg persisted and her plantar reflexes were still extensor.

She was reviewed by a neurologist 4 days later and there were now signs of a spastic paraparesis, with the right leg worse than the left, and bilateral extensor plantar reflexes. There was no clear sensory level, but sensation to pinprick appeared decreased below the sixth thoracic dermatomal level. The neurologist considered that the clinical picture was suggestive of a vascular cord lesion.

She improved gradually over the next week and was walking with the aid of a Zimmer frame when she was discharged on the 15th day after operation. She was able to walk with the aid of a stick and her lower limb reflexes were normal at 6 weeks. She had minimal weakness in her right leg after 6 months.

There are very few reports in the literature of neurological problems after general anaesthesia alone without a regional technique. Schriener *et al.* reported three cases of paralysis that occurred in one institution over a 12-month period, to give an incidence of 1 in 6000.[1] The respective causes were femoral neuropathy related to surgical positioning, a blood borne epidural abscess, and malignant tissue which invaded the spinal cord.

Postoperative paraplegia due to a spontaneous subdural haemorrhage has been reported.[2] A report of hemiplegia after appendicectomy in a 12-year-old was attributed to a septic embolus in the internal capsule. However, an air embolus was also considered as a possibility, as was an unrelated coincidental minor cerebrovascular accident.[3]

Spontaneous spinal cord infarction is well documented[4] and we can only assume that this was the aetiology in our patient, as the sudden onset and rapid improvement is suggestive of an embolic phenomenon. However, there is little evidence to support a source of emboli since serial ECGs and enzymes revealed no signs of myocardial infarction and the patient showed no tendency to arrhythmias whilst under anaesthesia or in the postoperative period. There was no period of hypotension during anaesthesia and no evidence of prolonged hypotension in the postoperative period.

Glenfield General Hospital,
Leicester LE3 9QP
A. Kitching
S. Taylor

References

1. Schreiner EJ, Lipson SF, Bromage PR, Camporesi EM. Neurological complications following general anaesthesia. Three cases of major paralysis. *Anaesthesia* 1983; **38:** 226–9.
2. Newbery JM. Paraplegia following general anaesthesia (letter). *Anaesthesia* 1977; **32:** 78–9.
3. McCormick MV, Heydenrych JJ, Le Roux JL. Hemiplegia—an unusual complication of appendectomy. A case report. *South African Medical Journal* 1987; **71:** 790–1.
4. Henson PA, Parsons M. Ischaemic lesion of the spinal cord: an illustrated review. *Quarterly Journal of Medicine* 1967; **36:** 205–22.

Headache after dural puncture

The paper on this subject by Dr Flaatten *et al.* (*Anaesthesia* 1989; **44:** 147–9) was interesting since I have recently completed a study of 100 consecutive spinal anaesthetics in obstetric patients randomly allocated to a 25- or 26-gauge needle group. All had lumbar puncture in the right lateral position with the bevel of the needle parallel to the dural fibres. Isobaric bupivacaine 2.5 ml were injected after cerebrospinal fluid appeared at the needle hub. The needle was withdrawn and the patients were then placed, wedged to the left for the obstetric procedure. Intravenous fluids were continued for a minimum of 6 hours after operation and the patients were nursed flat with one pillow, until power in their legs had returned to normal. All patients were seen 24 and 48 hours later and were interviewed in a standardised manner to ascertain the occurrence of headache. A headache that was severe, worse on standing or straining and relieved by lying down was defined as headache after dural puncture. Patients who had a severe headache were offered an epidural blood patch. The results were analysed using the Chi-squared test and Fisher's exact test as appropriate.

The incidence of headache was 18% in the 25-gauge group and 2% in the 26-gauge group (Table 1). There were no failed blocks in either group. These results compare favourably with those of Dr Flaatten *et al.* who found an incidence of headache after dural puncture of 10.1% with 26-gauge needles and none using 29-gauge needles (but dural puncture failed in 8% patients). The only headache that developed in a patient lasted one day and only required simple analgesia in my series.

Table 1. Needle size, headache and epidural blood patch.

	Gauge of needle					
	25	26	25	26	25	26
Procedure	No. of patients		No. with headache		No. of blood patches	
Keilland's forceps	18	18	4	1	3	0
Retained placenta	19	15	3	0	2	0
Lower segments Caesarean section	15	16	2	0	1	0
Total	51	49	9	1	6	0
	ns		p<.05		p<.05	

The ease and certainty of dural puncture with a 26-gauge needle combined with low incidence of headache makes 26-gauge needles a suitable choice when delay is undesirable.

Morriston Hospital,
Swansea SA6 6NL
P. Barker

A reply

Thank you for the opportunity to comment on the letter from Dr Barker. His observations in obstetric patients given spinal anaesthesia fit nicely with what long ago was regarded as definitively proven: the smaller the needle, the less the incidence of postdural puncture headache (PDPH). Franksson and Gordh[1] as early as 1946 observed a reduced frequency of PDPH with 0.5-mm needles (26-gauge).[1] Interestingly, obstetric patients do not seem to have a greater incidence of PDPH than nonobstetric patients of the same age (even though no randomised study of this exists). Brownridge,[2] in a study of 442 women given spinal anaesthesia for different obstetric procedures, found the frequency of PDPH to be 8.6% with either 25- or 26-gauge needles. Ten patients (2.3%) received an epidural blood patch. Unfortunately, Brownridge does not give data about PDPH between these two needles. We have recently reported PDPH in four of 50 women[3] in a study where spinal anaesthesia was given with a 26-gauge needle for Caesarean section. The headache was relieved by oral analgesics, and the duration of hospital stay was not increased. Spinal anaesthesia using 26-gauge needles is easy to perform after training, even without an introducer. The expected frequency of PDPH in obstetric patients using such thin needles can be well under 10%. The headache seems to be mild and does not require an epidural blood-patch in most cases. The superiority of spinal anaesthesia over both epidural and general anaesthesia in many obstetric settings, makes this a very attractive alternative, given that the patient is not hypovolaemic.

Central Hospital,
6800 Førde,
Norway
H. Flaatten

References

1. Franksson C, Gordh T. Headache after spinal anesthesia and a technique for lessening its frequency. *Acta Chirurgica Scandinavica* 1946; **94:** 443–54.
2. Brownridge P. Spinal anaesthesia revisted: An evaluation of subarachnoid block in obstetrics. *Anaesthesia and Intensive Care* 1984; **12:** 334–42.
3. Flaatten H, Tjugum J. Spinal anaesthesia for Caesarean section. *Tidsskrift for den Norske Lægeforening* 1988; **108:** 2965–7.

Propofol and fentanyl anaesthesia

In a similar study to that of Dr Russell and colleagues (*Anaesthesia* 1989; **44:** 205–8) we have infused propofol during cardiac surgery and measured whole blood propofol concentrations. Our results were in keeping generally with those presented, but we did not detect a decrease in propofol concentration after the start of extracorporeal circulation. This may be because we did not sample from the oxygenator during cardiopulmonary bypass but sampled from the radial artery of the patients throughout. The effective volume of distribution of propofol in these two systems is very different [3 litres in the pump; 800 litres in patients (our study)] so the change in whole blood propofol concentration in response to acute volume changes detected when sampling from one or other system may be of different magnitude and rate. Six correlation samples were taken in Dr Russell's study from the two sites; however, the sampling times are not quoted: if these did not coincide with the initial period of mixing (2 to 10 minutes), but were taken when the two systems had approached equilibrium, then the validity of the early decrease after the start of cardiopulmonary bypass must be in doubt.

The method described for measuring *in vitro* plasma binding does not correlate with the *in vivo* binding samples. In the *in vitro*, propofol was added to plasma only whereas *in vivo* whole blood-containing propofol was sampled and the plasma separated. The effect of heparin on red cell drug binding may be important.

The authors ascribe the increase in concentration after bypass to retransfused pump blood. This contained about 3 mg of propofol/litre which represents 1.3% of the hourly infusion to their average patient (i.e. 227 mg/hour for a 75.6 kg man): this is an amount unlikely to cause a detectable increase in blood propofol concentration. A more plausible explanation is that propofol is sequestered in sites within the body such as the lungs during cardiopulmonary bypass and is subsequently released.

Northern General Hospital,
Sheffield S5 7AU

K.M. Sherry
N.J.A. Massey
C.S. Reilly

A reply

Thank you for the opportunity to discuss some of the points made by Dr Sherry and colleagues.

Whole blood was sampled from the radial artery during the early normothermic mixing phase of bypass. Subsequent samples were then taken from the pump arterial line, with the validity established during early hypothermia and during rewarming. We are therefore surprised that a decrease in propofol concentration was not detected with the onset of cardiopulmonary bypass (CPB), which was a uniform finding. The three litres of compound sodium lactate solution used to prime the pump is initially confined to the central circulation, rather than to the entire distribution volume of propofol. This acute haemodilution causes a concentration gradient between blood and tissues. The distribution half-life of propofol is short (2–4 minutes), but equilibration will not be instantaneous and early sampling revealed the transient decrease in drug concentration at this time. Etomidate, with a short distribution half-life and large steady-state volume of distribution,[1] has been shown to behave in a similar way at the onset of bypass.

The effect of heparin on the red cell binding of propofol was not established in our study. Any action of heparin in this respect would either increase or decrease the total drug concentration in the separated plasma of the *in vivo* samples. Protein binding studies with the dianorm-equilibrium technique show constant results (around 98% binding) up to a propofol concentration as high as 20 μg/ml, well beyond the range seen in our patients. It is therefore unlikely that any effect of heparin on red cell binding would significantly alter our protein binding results.

A number of factors may account for the gradual increase in propofol concentration following CPB. As Dr Shelly suggests, any drug stored in the lungs will be redistributed when the pulmonary circulation is restored. This might be expected to produce a small secondary peak in concentration due to exponential washout, rather than the gradual rise we noted. Additional factors may include a reduction in propofol clearance due to the after-drop in core temperature that occurs following hypothermic CPB.

Broadgreen Hospital,
Liverpool

G.N. Russell

Reference

1. Arden JR, Holley FO, Stanski DR. Increased sensitivity to etomidate in the elderly: initial distribution versus altered brain response. *Anesthesiology* 1986; **65:** 19–27.

The choice of anaesthesia for the very old

We read with interest the paper by Dr Hosking and his associates (*Anaesthesia* 1989; **44:** 142–7). There are three main points that we wish to make.

It is essential in a study of this nature that the status before operation of the relevant groups of patients should be similar. We applaud the comprehensive medical record system of the Mayo Clinic, but it is highly doubtful that their study groups were comparable. Even if we were to accept that successive generations of internists over the 11-year study period were able to achieve a sufficient level of consistency in diagnosis and ASA physical status classification, it is still probable that there are real differences between the general (GA) and regional anaesthesia (RA) groups. For example, the authors have drawn attention to the increased pre-operative incidence of angina and arrhythmias in the RA group who had transurethral resection of the prostrate (TURP). What are we to make of the 28.5% difference in incidence of 'previous cancer', the 9.7% difference in incidence of 'previous endocrine disease', and the fact that 20.4% of GA patients who had total hip arthroplasty (THA) were classified as ASA 4 compared with 31.6% in the RA group? Failure to demonstrate that differences such as these were 'statistically significant' does not, of course, rule out the possibility that real differences which may have affected outcome exist (*vide infra*).

Did the patients who had regional anaesthesia receive concurrent intravenous sedation and if so to what extent?

The numbers of patients in this study (THA: RA=38, GA=103; TURP: RA=31, GA=13) are inadequate. This may be illustrated by following the authors' line of reasoning in their discussion on the possible significance of the increased incidence of arrhythmias before operation in the RA group on the 1-year postoperative mortality for the two groups of patients. As indicated, a 50% increase in mortality in the GA group would lead to a 41% mortality in this group compared with 33.8% in the RA group. This would indeed not be statistically significant with the numbers involved in this study, but a randomised study would require 946 patients per group, with 90% power and 5% Type I error rate to demonstrate such a difference. Even a 100% increase in mortality in the GA group resulting in a 54.6% mortality compared with 33.8% in the RA group (a not insubstantial difference) would still produce a nonsignificant result, and a randomised study would require 233 patients per group for a proper evaluation.

If we assume comparability of the study groups, it is possible to calculate the 95% confidence interval for differences in either mortality or morbidity between the two anaesthetic groups for TURP or THA patients. Such calculations would, in the main, show that the data are compatible with either substantial benefits of general anaesthesia over regional, substantial benefits of regional anaesthesia over general or no difference at all.

The relative merits of RA or GA for operative procedures in the elderly has been the subject of several studies which have produced conflicting results. Dr Hoskings and his associates have provided useful information on outcome following THA and TURP in the very elderly patient, but the data presented do not justify their conclusion that anaesthetic technique did not influence short-term morbidity and mortality or long-term outcome.

St Thomas' Hospital,
London SE1 7EH

M. Lim
D.N. Campbell
R. Morris

A reply

The comments by Drs Lim, Campbell, and Morris are noteworthy, and apply not only to our study but many others. We respond to their questions in the order in which they were posed.

It would clearly be an error to imply that patients in the regional and general anaesthesia groups in this retrospective study were identical in all ways. We agree that lack of statistical significance does not ensure comparable groups, and it was for this reason that we included several extensive tables to allow readers to make their own appropriate clinical judgements.

However, comparability would not be assured short of a randomised, controlled trial. A randomised prospective study is always desirable, but efforts to study rare events in small patient populations may be nearly impossible, as the writers themselves point out in their third comment. Moreover, there is one particularly admirable strength achieved only by a retrospective study: it 'tells it like it really happened'. The elderly individuals in our study received the type and quality of care that the staff anaesthetists at the Mayo Clinic believed to be best for those patients at that time. Patients studied prospectively, in contrast, often receive more attention than patients ordinarily do. The results of prospective studies may not therefore always reflect actual practice.

All patients who had total hip arthroplasty who received a regional anaesthetic were given concurrent intravenous sedation in the form of narcotics and (or) benzodiazepines. Thirty-five percent of patients undergoing transurethral resection of the prostate with regional anaesthesia received sedation. These drugs were titrated with appropriate monitoring according to the judgement of the individual anaesthetist in all cases with sedation.

The optimal method of addressing the regional versus general anaesthesia controversy in this aged population would be a prospective randomised trial. However, the likelihood of a single institution or even several institutions undertaking a coordinated prospective study of nearly 2000 patients over 90 years of age seems remote. The number of patients in this retrospective review is by far the largest series ever reported in this age group and, despite the fact that we have a very large practice (approximately 60 000 operations per year), it took 11 years to accumulate this number of elderly patients. Consequently, it seems inevitable that, for the time being, conclusions must be based upon this and similar retrospective studies.

Finally, overall outcome and long-term survival was surprisingly good in these elderly patients, and age alone need not be a barrier to surgery. Given the best care that staff anaesthetists at the Mayo Clinic could provide these patients aged 90 years or more from 1975 through 1985, we failed to detect any significant differences in peri-operative major morbidity or mortality between patients who received regional versus general anaesthesia for total hip arthroplasty or transurethral resection of the prostate.

Mayo Clinic,
Rochester,
Minnesota 55905,
USA

M.P. Hosking
C.M. Lobdell
M.A. Warner
K.P Offord
L.J. Melton

Asystole on induction

The report about this (*Anaesthesia* 1989; **44:** 354–5) was interesting. Several hours after reading it, a similar event occurred to a patient under my care but under somewhat different circumstances.

A 34-year-old fit unpremedicated ASA 1 woman presented for an emergency laparoscopy/laparotomy for a suspected ectopic pregnancy. Her pre-induction blood pressure was 100/60 mmHg, the heart rate 70 beats/minute and she was warm peripherally; nevertheless anaesthesia was induced in the operating room with full monitoring because she looked far more ill than these physical signs suggested.

Induction of anaesthesia was carried out in rapid sequence after pre-oxygenation and during the application of cricoid pressure. The drugs used were etomidate 20 mg and suxamethonium 100 mg, after which tracheal intubation was performed promptly. Soon after cuff inflation, with mechanical ventilation of the lungs established, the ECG monitor showed the occasional dropped beat. Seconds later this proceeded to asystole. Cardiac massage was started and atropine 0.6 mg given. An idioventricular rhythm was seen, with electromechanical dissociation and a rate of 25/minute. This soon reverted to sinus rhythm at 100/minute, with normal pulses.

Surgery commenced and the ectopic pregnancy was removed under a subsequently uneventful anaesthetic. The patient was transferred awake and extubated to the intensive therapy unit for postoperative monitoring, which was unremarkable. There were no positive findings in any of the investigations performed.

No vagotonic drugs were used before the occurrence of the arrhythmia, unlike the cases reported in the letter referred to above. Given the sympathetic overactivity more likely to be present at such a time, as a result of pain, blood loss and anxiety, it is more difficult to suppose a cause for the events seen.

Whether or not these events would have resolved spontaneously will never be known. The implementation of minimum monitoring requirements will bring to light the true incidence of such occurrences.

Queen's Medical Centre,
Nottingham NG7 2UA
K. Ruiz

Anaesthesia in myotonia dystrophica

A 29-year-old, 71-kg man presented for drainage of a perianal abscess. Premedication was with lorazepam 2 mg and he was anaesthetised using propofol, fentanyl, atracurium, nitrous oxide, oxygen and halothane, with controlled ventilation of the lungs. The surgery lasted 40 minutes. No problems were encountered and he awoke immediately anaesthesia was discontinued. One week later he required further surgery. A different anaesthetist used a different technique on the second occasion. Premedication was with papaveretum 15 mg and hyoscine 0.3 mg and he received thiopentone 200 mg, etomidate 16 mg, and suxamethonium 60 mg, followed by nitrous oxide, oxygen and isoflurane through the tracheal tube. The patient remained apnoeic throughout the whole operation and into the recovery period, which necessitated the use of continued controlled ventilation of the lungs. A nerve stimulator demonstrated that the action of the suxamethonium had ended. Naloxone 0.4 mg and doxapram 100 mg, were given with no response. The patient began to breathe and to awaken slowly after a delay of about 40 minutes. He made a full recovery, and upon close questioning the next day described a previous episode of being slow to recover after a previous anaesthetic. He also now gave a family history of myotonia dystrophica which he had not previously thought important because he was only mildly affected. His sister was also mildly affected, but their father had been more severely affected, as were his sister's children.

Patients with myotonia dystrophica present a problem for anaesthesia. They are very sensitive to thiopentone, opiates and other respiratory depressants, and a prolonged period of controlled ventilation may be needed until the depressant effect has worn off.[1] It seems likely that it was thiopentone which was responsible on this occasion. The etomidate which was also given in combination for induction (routine practice of this anaesthetist) cannot however be excluded as a contributory factor. Patients with myotonia dystrophica are also sensitive to opiates, although this patient received opiates on both occasions and had previous administration of papaveretum for analgesia on the ward without problems. The interesting point to note from this case is that propofol was used for his first anaesthetic, with rapid recovery, and it appears from this comparison of two techniques in the same patient that propofol may be a more suitable choice of induction agent for patients with myotonia dystrophica. There are a number of other considerations when administering anaesthesia to patients with this condition. The use of suxamethonium is unwise since it may induce a myotonic reaction, although no problems were encountered here. The importance of an accurate family history is emphasised as well as that of the education of patients in relation to their illnesses. This patient was interviewed and supplied with a warning card.

Manchester Royal Infirmary,
Manchester M13 9WL
B.J. Pollard
T.M. Young

References

1. Aldridge L. Anaesthetic problems in myotonia dystrophy. *British Journal of Anaesthesia* 1985; **57**: 1119–30.

Failure of Heimlich manoeuvre

The use of abdominal infradiaphragmatic pressure for the treatment of food choking was first described by Heimlich in 1974.[1] This technique has since become a widely advocated life-saving manoeuvre for choking.[2] Fractured ribs are a complication of the technique and, Heimlich emphasised that the rescuer must apply the pressure with his fist below the rib cage.[3] Visintine and Baick[4] reported a case of gastric rupture after application of the Heimlich manoeuvre. The manoeuvre may be unsuccessful in some cases on the first and second attempts;[5] there are no reports in the literature of complete failure of the manoeuvre.

We report a patient in whom repeated attempts at the Heimlich manoeuvre failed to dislodge a foreign body impacted in the glottis. A 74-year-old man, with a history of multiple cerebrovascular accidents and right hemiplegia, was lunching at home when suddenly he appeared to choke. The ambulance officers attending the emergency call made the correct diagnosis of airway obstruction and performed the Heimlich manoeuvre without effect. Attempts at digital extraction of the foreign body were unsuccessful. The patient was semiconscious and dyspnoeic (but not cyanosed) on arrival at the Accident and Emergency Department, with a pulse rate of 130 beats/minute and a systemic arterial pressure of 180/60 mmHg. Renewed attempts at Heimlich's manoeuvre were unsuccessful. Direct laryngoscopy revealed a thick wad of whitish material in the posterior pharynx which extended caudally through the vocal cords, partially obstructing the trachea. There was immediate symptomatic relief on retrieval of this with the aid of Magill's forceps. The wad was found to be a paper tissue handkerchief which was sodden with saliva.

Heimlich's manoeuvre causes sudden elevation of the diaphragm, and thus compresses the lungs within the confines of the rib-cage, and increases the tracheobronchial air pressure.[6] This pressure ejects the obstructing bolus. The manoeuvre can be equally successful in both partial and complete obstruction of the trachea.[7]

It was discovered in a study of 10 healthy, conscious adult volunteers,[7] who breathed into a closed system with a recording spirometer, that, when the manoeuvre was applied, the peak expiratory flow rate obtained was 205 litres/minute with 940 ml of air expelled during the early expiratory phase, at a pressure of 4.1 kPa (mean values). The effect of the manoeuvre was studied in anaesthetised beagles[7] when each application caused 120 ml to be ejected (the animal's normal tidal volume). However, in beagles paralysed with tubocurarine, the volume exchange decreased to levels of 20 to 40 ml within 30 seconds of repeated applications. Heimlich theorised that the paralysed diaphragm is unable to descend to its original position in these circumstances and results in a reduction of the air volume after each application of the manoeuvre.

It is possible that, in this patient with hemiplegia and reduced lung volume, diaphragmatic incompetence resulted in a rapid and progressive decrease in thoracic volume, which prevented the generation of sufficient airway pressure to dislodge the partial laryngeal obstruction.

This case highlights that all that is swallowed at meal times is not necessarily food and it demonstrates the likelihood of failure of the Heimlich manoeuvre in patients with reduced thoracic volume and diaphragmatic incompetence.

The Alexandra Hospital,
Redditch B98 7UB

P. Sagar
J.S. Goodman

References

1. Heimlich HJ. Pop goes the cafe coronary. *Emergency Medicine* 1974; **6:** 154–5.
2. Heimlich HJ. The Heimlich manoeuvre. *British Medical Journal* 1983; **286:** 1349–50.
3. Heimlich HJ. A life-saving maneuver to prevent food-choking. *Journal of the American Medical Association* 1975; **234:** 398–401.
4. Visintine RE, Baick CH. Ruptured stomach after Heimlich maneuver. *Journal of the American Medical Association* 1975; **234:** 415.
5. Mason MA. Letter. *British Medical Journal* 1983; **286:** 1350.
6. Donegan JH. Cardiopulmonary resuscitation. In: Miller RD, ed. *Anesthesia,* 2nd edn. New York: Churchill Livingstone, 1986: 2111–47.
7. Heimlich HJ, Hoffmann KA, Canestri FR. Food-choking and drowning deaths prevented by external subdiaphragmatic compression. Physiological basis. *Annals of Thoracic Surgery* 1975: **20:** 188–95.

A 10-second convulsion during propofol injection?

A 23-year-old man was scheduled for arthroscopy of his knee under general anaesthesia as a day case. He had no previous illnesses (no epilepsy), was otherwise asymptomatic, fasted and apyrexial, and had received no premedication. Induction of anaesthesia was with propofol, of which 200 mg was the anticipated requirement. He closed his eyes after 100 mg and stopped talking. He exhibited generalised myoclonic jerks soon after such as are commonly seen with etomidate. Injection was continued, but the jerks progressed to resemble closely a clonic grand mal convulsion. All four limbs and the patient's head were shaking violently. Injection was still continued, slowly, and after 10 seconds the convulsion stopped abruptly. The patient opened his eyes, gazed around, then closed his eyes again and progressed to an adequately deep plane of anaesthesia. Two hundred milligrams of propofol were given.

Anaesthesia was continued uneventfully using nitrous oxide, oxygen, halothane and alfentanil. The patient recovered rapidly, lucidly, and was discharged home later that day, after a very satisfactory recovery. Further questioning revealed no family history of epilepsy, and the patient had no recall of the episode. There was no tongue bite or incontinence, but this reaction was much more severe than the shakes after etomidate, and closely resembled a grand mal convulsion. The convulsion began and ended during injection of propofol, in the absence of any other drugs.

The association between propofol and convulsions is disputed. Propofol was shown to produce epileptiform electroencephalogram discharges in patients with intractable temporal lobe epilepsy, even in areas not previously mapped as epileptiform foci in these patients,[1] and another report mentions a postoperative seizure with possible propofol association.[2] The reports suggest that propofol is a proconvulsant. However in contrast, propofol in electroconvulsive therapy is associated with shorter convulsion duration than methohexitone,[3,4] and propofol has also been used to terminate intractable status epilepticus in a patient with Coxsackie B encephalitis.[5] This case may further fuel the controversy; however, if the case described here concerned 'just' myoclonic jerks, then they were very severe.

Royal Hallamshire Hospital,
Sheffield S10 2JF

I.H. Herrema

References

1. Hodkinson BP, Frith RW, Mee EW. Propofol and the electroencephalogram. *Lancet* 1987; **2:** 1518.
2. Cameron AE. Opisthotonus again. *Anaesthesia* 1987; **42:** 1124.
3. Rouse EC. Propofol for electroconvulsive therapy. A comparison with methohexitone, Preliminary report. *Anaesthesia* 1988; **43:** (Suppl.) 61–4.
4. Simpson KH, Halsall PJ, Carr CME, Stewart KG. Seizure duration after methohexitone or propofol for induction of anaesthesia for electroconvulsive therapy. (Abstract). *British Journal of Anaesthesia* 1987; **59:** 1323–4P.
5. Wood PR, Browne GPR, Pugh S. Propofol infusion for the treatment of status epilepticus. *Lancet* 1988; **1:** 480–1.

Costs of replacement of anaesthetic equipment

The paper by Schofield (*Anaesthesia* 1988; **43:** 883–6) which detailed the projected cost of replacement of anaesthetic equipment in a large Health Authority was interesting. He is quite correct in his conclusion that the problems which the Oxford Hospitals faced in 1986 were not unique. Judging from Dr Schofield's figures, Leeds Western Health Authority is about three-quarters of the size of the Oxford Health Authority. The equipment purchasing programme in Leeds West has been underfunded for at least a decade, with a shortage of money particularly for equipment that costs between £500 and £7500. Thus, for at least 10 years, anaesthetic equipment had been purchased by a system of crisis management. New anaesthetic machines and ventilators were only bought when old ones were beyond repair. Ventilator alarms were obtained after comments by the coroner after an unfortunate diasaster, and sufficient ECG monitors to allow their use on all anaesthetised patients were provided only under threat of curtailment of the anaesthetic service.

Our campaign for better funding for equipment began in

1983 when the Administration asked all Divisions to provide a Strategic Plan. This gave us the opportunity to stress the need for adequate funding to replace ageing equipment and achieve an acceptable standard of patient monitoring. However, the system of crisis management continued. A report (1985) from the Faculty of Anaesthetists of the Royal College of Surgeons on General Professional Training in Leeds West, which severely criticised the lack of adequate equipment for monitoring anaesthetised patients, and a combined approach with the Division of Medicine who faced a similar problem, persuaded Management to give a single allocation of £70 000 for anaesthetic equipment. The size of this allocation allowed us to negotiate a 25% discount on the list price of the monitoring equipment which we bought, and allowed the purchase of more equipment with the available funds. This enabled us to retain our Faculty Recognition for training, but the acquisition of new equipment is still based on crisis management and, despite repeated approaches to Management, we have not achieved our aim of adequate funding for a rolling replacement and development programme for anaesthetic equipment. However, when extra money becomes available, Management will give anaesthetic equipment a higher priority than previously, and they allocated extra money to our division in 1988/89.

We have learnt that to obtain the equipment needed in a Department of Anaesthetics it is necessary to have a consensus decision about what equipment is required at every site where anaesthetics are given, (a decision which is more easily made since the Association of Anaesthetists published its Recommendations for Standards of Monitoring during Anaesthesia and Recovery), and to request all of this equipment at the same time. It is pointless to make more modest requests because this gives Management the wrong impression about the funding required to equip to acceptable levels. We have also found that it is a mistake to combine the equipment requirements for the Division of Anaesthetics with those for Intensive Care. The Intensive Care Unit provides a service not only for us but for all other acute specialties and more money is forthcoming if the two services are separated.

It is essential for good equipment management to have a rolling replacement and development programme for anaesthetic equipment. In order to manage this a good, up-to-date, easily accessible inventory of the equipment is required. The useful life of most items of electronic equipment is 7 to 8 years, and of electromechanical and mechanical devices 15 years. It is possible with these facts to work out on 1989 prices the annual requirement for funding of items of equipment costing more than £500. This totals £101 000 for the anaesthetic equipment alone in Leeds Western Health Authority. Obviously the amount needed each year will vary because much of the monitoring equipment was bought and will reach the end of its useful life at the same time. It is possible to alleviate this problem by good forward planning. Replacement of several similar items of equipment at the same time allows bulk purchases and the negotiation of large discounts. However, there is a danger that funding surpluses may have to be spent on items which are not essential in order to spend the complete allocation for one financial year, whilst another year there is insufficient funding for all the essential purchases. Therefore, it is important that provision is made to save money and carry it over to the next financial year. It is also important that funding is increased in line with the increasing cost of equipment.

Surely it must be the aim of all Anaesthetic Departments to establish an adequately funded equipment purchase programme which takes into account replacement of ageing equipment and purchase of the new equipment which is required as anaesthesia continues to develop. An annual allocation of sufficient funds is required in order to do this, preferably as a Departmental Equipment Budget, with annual adjustment for inflation and provision for carrying money over to the next financial year. Our experience suggests that this will only be achieved by making Management aware of the size of the problem and reminding them regularly until they provide adequate funding.

The General Infirmary at Leeds
Great George Street,
Leeds LS1 3EX
E. MOSS

Keeping the position of the 29-gauge spinal needle

Flaatten *et al.* (*Anaesthesia* 1989; **44:** 147–9) have demonstrated that there is little risk of headache after dural puncture when a 29-gauge spinal needle is used. The availability of this needle as a sterile disposable product now makes it difficult to justify the continued use of larger gauge needles in young adults.

The incidence of postoperative headache of any kind was studied in a consecutive series of 138 mothers delivered by Caesarean section in Aberdeen after spinal anaesthesia with a 29-gauge 9-cm needle. A questionnaire was given to the mothers for completion on the fourth or subsequent days after operation. Specific questions on day of onset, days of occurrence, relief in the supine posture and severity were included. No headaches of any kind were experienced by 106 mothers. Various headaches of short duration were recorded by 20 mothers. Two mothers had a headache which was relieved by lying down and which lasted more than one day. It was recorded in one case as bearable and lasted 2–3 days, and in the other it was recorded as slight and lasted 1.5 days. A completed questionnaire was not received from 10 mothers.

The malleable characteristics of the 29-gauge make it essential for the introducer needle to reach close to the ligamentum flavum. The 3.1 cm introducer is sufficiently long for most patients. It is, however, useful to have available a small supply of 22-gauge 6.4 cm spinal needles to act as introducers for patients with thick backs.

The correct placement of the 29-gauge needle is probably best confirmed by aspiration of cerebrospinal fluid with a dry 2-ml syringe. The change from the tester syringe over to the syringe with local anaesthetic may result in inadvertent movement of the needle within the introducer. It is not easy

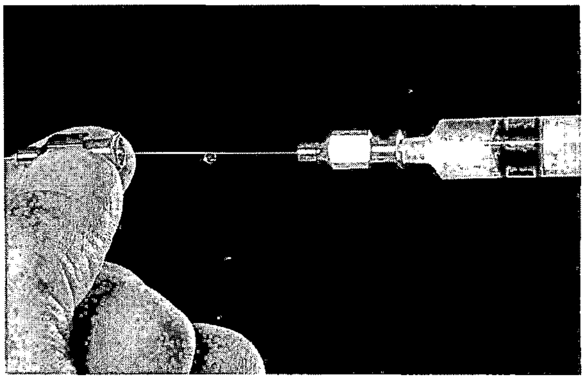


Fig. 1. Dew-drop position marker for the 29-gauge spinal needle.

to return exactly to the, previously confirmed, correct position of the needle. Memorising the original hub-to-hub distance of the exposed shaft of the 29-gauge needle is difficult. It is easier, however, to memorise the relative proportions of two distances on either side of a mark placed on the shaft of the needle. The most convenient way to mark the shaft of the spinal needle is to place a small dew-drop of liquid (local anaesthetic) on it. This is shown in the photograph made by Mr K. Duguid, Director of the Department of Medical Illustration, University of Aberdeen and his assistants. The dew-drop is wiped on to the shaft from the point of a subcutaneous needle from which a tiny droplet is extruded. The smaller dew-drops do not roll down the shaft of the needle even when this is held vertical.

Aberdeen Maternity Hospital,
Aberdeen AB9 2ZA

M.E. Tunstall

Debris in a breathing system

A potential hazard arising from the use of heat and moisture exchanging bacterial filters in conjunction with the Siemens Servo 900C ventilator was reported from this unit.[1] We recently had another problem related to this practice.

A patient whose condition made spontaneous respiratory activity impossible was receiving controlled ventilation when it became apparent that the expired minute volume appeared to be excessive. Previous similar episodes led us to suspect malfunction of the expiratory flow transducer. A different ventilator was substituted whilst the problem was investigated.

Inspection of the transducer revealed pieces of debris lodged in the fine mesh net (Fig. 1). Previous experience made us wonder if the patient Y-piece filter might be responsible. A similar sized piece was removed from a new filter and photographed for comparison (Fig. 2).

We have used Pall Ultipor heat and moisture exchanging filters (BB50T) since December 1987 in the place of heated water humidifiers and heated bacteriological filters on our Servo 900B and 900C ventilators. We modified our practice after our earlier report to include a second filter in the expiratory limb, in addition to the usual patient Y-piece filter, but recently reverted to the use of a single Y-piece filter after repeated assurances from the manufacturers that only one filter is necessary. The event described above took place within one week of the reversion. There were no problems during the period when two filters were employed.

We have hitherto accepted that modification of breathing systems for the administration of nebulised drugs might permit the introduction of foreign material. However, in this particular case, no nebulised agents were used, and the only reason to open the patient system was to perform tracheal suction, when a complete disconnexion was made between the catheter mount and the tracheal tube.

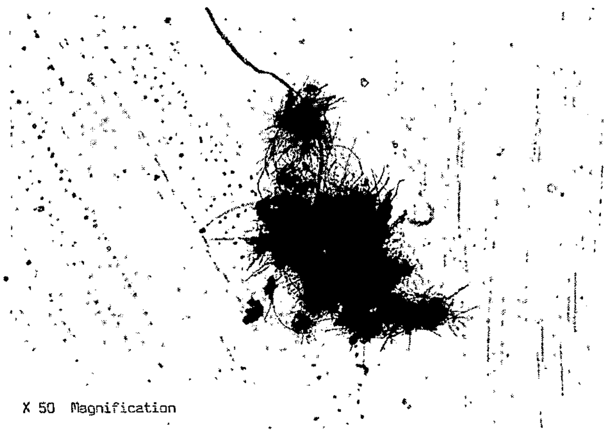


Fig. 1.

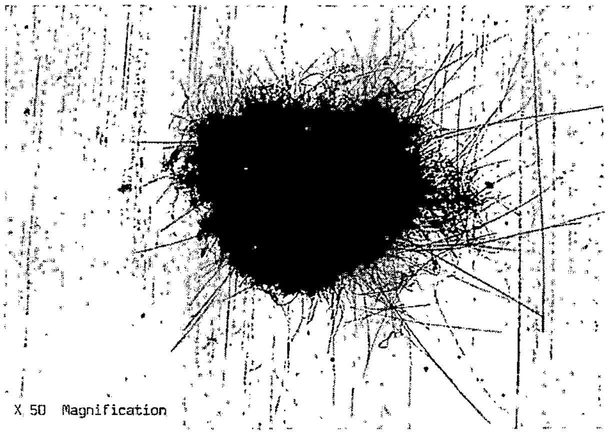


Fig. 2.

It is impossible to be certain that the debris collected on the transducer originated from the filter, but the photographic appearances of the debris and the filter material are strikingly similar. The implications of this are worrying.

Bristol Royal Infirmary,
Bristol BS2 8HW

B.L. Taylor
C. Rainbow
D. Ford

References

1. Kong KL, Rainbow C, Ford DB. Heat and moisture exchanging bacterial filters. *Anaesthesia* 1988; **43:** 254.

A reply

We have been actively investigating the observations of Dr Taylor and his colleagues at Bristol Royal Infirmary since their first report of unexplained transducer mesh contamination. Since that time we have evaluated three individuals transducer meshes supplied to us by that hospital.

The first mesh became available to us some months after the reported observations. Scanning electron microscopy (S.E.M.) revealed that the contaminants were fibrous in nature, while spectrophotometric analysis suggested that they were probably organic. There were no signals corresponding to the media in the Pall Ultipor filter. Unfortunately, the analytical techniques did not allow a complete identification of the small sample of fibre present and so we were unable to comment on their source.

The second mesh examined was reported to us as showing increased resistance which resulted in the large expired minute volume reading Dr Taylor, Sister Rainbow and Mr Ford describe. A variety of contaminants were found on the mesh including glass fibre, cellulose and other organic fibres (including coloured fibres which may have arisen from nursing or medical garments). Interestingly, the mesh was also found to be 70% occluded by sodium chloride crystals which almost certainly explains the resistance change. It is noteworthy that the third mesh which was not removed as a result of resistance changes, but at a routine service change, did bear fibrous material but the pressure difference across the mesh was normal.

It was suggested to us that the groups' observations were related to the use of the filter as a heat and moisture exchanging filter (HMEF) since no problems were experienced when the filter was placed on the ventilator expiratory port. The authors proposed that perhaps the HMEF was stressed and shed fibres. We have subjected the filter to extensive tests in the course of research and development and continue to monitor filter integrity with 100% in-manufacture testing, but we set up a further experiment under the supervision of the Bristol group in our laboratories. No fibres were detected on a transducer mesh placed in the expiratory line after a period of 12 days with a filter change in excess of normal recommended use times (to increase the severity of the test).

We have also visited the unit in which these observations were made, and have found that the normal practices of the unit for ventilated patients make it very difficult to pinpoint the potential exposure of the transducer mesh to a single manufacturer's filter. Two types of breathing systems are used in conjunction with the Servo 900B and 900C ventilators.

Type A has inspiratory tubing, expiratory tubing, Y-piece, Pall HMEF, catheter mount (and since the observation of transducer contaminants an additional Pall filter has been placed on the expiratory port).

Type B has inspiratory tubing plus water trap, water bath humidifier with blotting paper insert (cellulose), Y-piece, catheter mount, expiratory tubing plus water trap, heated expiratory filter (Cape Microflow).

A type A system is often replaced with a type B system and, as such, a single transducer mesh is exposed to both types of filter. Analysis suggests that the substrate of the media fragments from the Cape filter give similar readings to Pall media, except that hydrophobic resins are not present.

We agree with Dr Taylor and his colleagues that it is impossible to be certain that the debris collected on the transducer originated from the circuit filter. Other publications have indicated the filter to be a safe device for contamination control and effective humidification when used as an HMEF.[1,2]

We are engaged in work to identify the sources of the fibrous materials. These may include, for example, nebuliser drive line filters, tubing, inspiratory gases, inspiratory filter (built into ventilator), expiratory filters or HMEFs (Cape and Pall), the atmosphere (contamination by glass fibres and cellulose), humidifier (paper) and perhaps others. We believe however that the incident which resulted in transducer occlusion was due to blockage by saline crystals and was unrelated to the use of the filter.

However, we are not confident of our ability to identify a single source of what appears to be contamination from multiple origins.

Pall Biomedical Ltd,
Portsmouth,
Hants PO1 3PD

L. MARSHALL
G.D. LOWE

References

1. GALLAGHER J, STRANGEWAYS JEM, ALLT-GRAHAM J. Contamination control in long-term ventilation. A cinical study using a heat- and moisture-exchanging filter. *Anaesthesia* 1987; **42:** 476–81.
2. TENAILLON A, CHOLLEY G, BOITEAU R, PERRIN-GACHADOAT D, BURDIN M. Filtre echangeur de Chaleur et D'humidite' versus humidificateur chauffant en ventilation mecanique prolongie. *Réanimation et médecine d'urgence* 1989; **5:** 5–10.

Large tonsils and the laryngeal mask airway

An 80-kg, 18-year-old male presented for an elective orthopaedic procedure, and anaesthesia was induced with 160 mg propofol. We then attempted to place a laryngeal mask airway (LMA). However, it was not possible to advance the LMA into the pharynx, despite good lubrication and three attempts. We assumed the reason for the difficulty in placing the LMA was due to the patient being too 'light', with an active gag reflex, and a further 40 mg propofol was given. Pharyngeal placement again proved impossible. We decided at this stage to increase the depth of anaesthesia using inhalational agents (nitrous oxide, oxygen and isoflurane) before direct laryngoscopy to assess the airway. It proved difficult during this interval to maintain a clear airway using a facemask and an oropharyngeal airway was used. Once an adequate depth of anaesthesia had been established, direct laryngoscopy revealed very large pharyngeal tonsils protruding into the pharynx and showing some evidence of trauma from the attempts at LMA placement. Lifting the tongue anteriorly with the laryngoscope allowed passage of the LMA between the back of the tongue and the tonsils and a clear airway was established without further mishap. We conclude that the blind passage of the LMA into the pharynx is not without hazard and that if difficulty is experienced in placing it, direct laryngoscopy is indicated to assess the anatomy of the airway.

Royal Devon and Exeter Hospital,
Exeter,
Devon EX2 5DW

P.V. VAN HEERDEN
D. KIRRAGE

Chain of errors

Anaesthetic accidents, like air disasters, tend to occur as a result of a series of minor, uncorrected errors rather than a single major error.[1] The following is an example of a critical incident which illustrates the point.

A young man, previously fit, was admitted to the casualty department with a badly displaced Pott's fracture. There was some doubt about the adequacy of the circulation to the foot and therefore preparations were made for urgent open reduction and fixation. The author visited the patient in the casualty department and noted a fresh venepuncture mark in the antecubital fossa of the same arm in which an intravenous infusion was running. Nearby, the casualty officer was preparing to send off routine investigations. It was pointed out that the results of these would not be reliable. It was assumed, incorrectly, that the mistake would be remedied.

Shortly afterwards, the patient was anaesthetised in the casualty theatre. A rapid sequence induction with thiopentone and suxamethonium was carried out after pre-oxygenation, cricoid pressure applied and tracheal intubation performed. The patient was allowed to breathe nitrous oxide, oxygen and enflurane via the Magill attachment after recovery of neuromuscular function. The enflurane was supplied by a free-standing Enfluratec vaporizer connected to the Boyle's machine with flexible hoses and tapered metal connexions. The affected limb was exsanguinated, a pneumatic tourniquet applied and surgery commenced.

The author, who was required for a session in another hospital, was relieved after 45 minutes of uneventful anaesthesia by an SHO, supervised by a clinical assistant. A decision was made to change from spontaneous to controlled ventilation. Atracurium was administered and the patient connected to a Blease Manley ventilator, using the same anaesthetic gas mixture as previously. Neither a pulse oximeter nor a ventilator alarm was available in the theatre. The clinical assistant then adjourned leaving the SHO with the patient. A set of blood investigations arrived in theatre showing the serum potassium as 2.0 mmol/litre. Alarmed by the result, the SHO made preparations to repeat the test and started looking for a suitable vein from which to take blood. While he was busy and distracted, one of the tapered metal connectors to the vaporizer, which had evidently not been applied firmly, became detached. The disconnexion was perhaps precipitated by a degree of back-pressure from the ventilator. Fresh gas supply was cut off to the ventilator and ventilation of the lungs ceased. The patient was already cyanosed when, by good fortune, the clinical assistant returned and was immediately alerted by the absence of the ventilator cadence. Ventilation was restarted and the patient made an uneventful recovery without apparent neurological deficit.

Thus a series of errors lead to a potentially fatal incident. The deficits in monitoring in this theatre have now been corrected. The other errors are easily repeatable.

University Hospital of Wales
Cardiff CF4 4XN
R.W. Okell

Reference

1. Gaba DM, Maxwell M, De Anda A. Anesthetic mishaps: breaking the chain of accident evolution. *Anesthesiology* 1987; **66:** 670–6.

Embolectomy without bypass

An embolus of the fractured fragments of an intravenous catheter which requires to be removed surgically is an uncommon but recognised occurrence.[1,2] Reports of cases of catheter embolus by severance at the hub[3] and by knotting[4,5] have appeared in the literature. The contributing factor in the case of a child reported here was the age of the catheter which was well past its expiry date.

There is a danger when such catheters are used, especially in developing countries, where the cost of purchase of catheters and of inadequate funding of hospitals, for this type of accident to become more likely. There may be marked reduction in cardiac output and signs of myocardial strain when sudden death does not occur after catheter embolisation. Reul and Beall[6] decribed the ideal technique under cardiopulmonary bypass for pulmonary embolectomy but where bypass facilities are not available the catheter may be removed through a pulmonary arteriotomy. The risks associated with this procedure are obvious.

Premedication with atropine was omitted and a calculated dose of promethazine (12.5 mg) was administered. Induction was with intravenous diazepam (2.5 mg) after pre-oxygenation for 3 minutes followed by thiopentone and (1.5 mg) vecuronium; the lungs were ventilated until full relaxation developed. Tracheal intubation was then performed in an appropriate tube (4.5 mm); the pharynx was packed. Intermittent positive pressure ventilation (IPPV) of the lungs was started and maintained throughout the procedure. The patient was given 100% oxygen with 0.5% halothane for about 5 minutes before the pulmonary arteriotomy while IPPV continued. The catheter was found at the pulmonary trunk partly in the left main branch of the pulmonary artery. The catheter was removed through an arteriotomy in the more distal part of the pulmonary vessel and haemostasis was maintained during occlusion of the vessel. The period of occlusion was less than 3 minutes and the patient was kept in a slightly head down position to discourage air embolus. Reversal of muscular relation was followed by a prompt recovery during which 100% oxygen was given. The patient was discharged from hospital with no residual defects.

University College Hospital,
Ibadan,
Nigeria
P.T. Sotunmbi
S.D. Amanor-Boadu
A.A. Sanusi

References

1. Doering RB, Stemmer AE, Connolly JE. Complications of indwelling venous catheters, with particular reference to catheter embolus. *American Journal of Surgery* 1967; **114:** 259–66.
2. Wellman KF, Reinhard A, Salazar EP. Polyethylene catheter embolism. Review of the literature and report of a case with associated fatal tricuspid and systemic candidiasis. *Circulation* 1968; **37:** 380–92.
3. Sprague DD, Sarwar H. Catheter embolization due to faulty bonding of catheter shaft to hub. *Anesthesiology* 1978; **49:** 285–6.
4. Daum S, Shapira M. Intracardiac knot formation Swan-Ganz catheter. *Anesthesia and Analgesia* 1973; **52:** 862–3.
5. Lipp H, O'Donoghue K, Resnekou L. Intracardiac knotting of a flow-directed balloon catheter. *New England Journal of Medicine* 1971; **284:** 220.
6. Reul GJ, Beall AC, Emergency pulmonary embolectomy for massive pulmonary embolism. *Circulation* 1974; **50** (Suppl. II): 236–41.

Unusual cause of obstructed expiration

This is a report of an unusual cause of high pressure in a breathing system.

A patient's lungs were being ventilated with a Nuffield 200, driving a Humphrey system. An ECG electrode needed to be replaced so I got up from my chair. The ventilator alarm sounded within four or five breaths after I sat down. Manual ventilation revealed that the chest compliance felt normal; nothing untoward was detected by auscultation and the breathing system seemed to function normally so IPPV with a Manley ventilator was restarted without further problems.

On further examination, I discovered that the exhaust port of the Nuffield was obstructed by my chair which must have moved backwards when I stood up. This resulted in the patient being unable to exhale completely in the time allotted by the ventilator, and to the high pressure which triggered the alarm. The scavenging system, which otherwise would have prevented this sequence, was also displaced by my stool.

North Staffordshire Royal Infirmary,
Stoke on Trent
P. Johnston

The oesophageal detector device

We believe that Nunn's modification of the oesophageal detector device (*Anaesthesia* 1988; **43:** 804) is an invaluable aid to confirmation of correct placement of a tracheal tube and invariably apply it. However, we report a false positive result when the oesophageal detector device suggested oesophageal placement when in fact the tube was correctly positioned in the trachea.

A 77-year-old female with atlanto-axial instability, secondary to severe rheumatoid arthritis, was anaesthetised for a posterior cervical fusion. The patient had a thyromental (Patil) distance[1] of two fingers and was Mallampati[2] grade III. A nasal intubation was therefore carried out with the aid of a fibreoptic intubating bronchoscope. A good view of the carina was obtained and a 6 mm Portex nylon reinforced tube was easily passed over the fibrescope into the trachea. Nunn's modification of the oesophageal detector device was applied but the bulb of the Ellick's evacuator did not refill and thus indicated oesophageal intubation. The fibrescope was re-inserted through the tracheal tube and tracheal placement confirmed, but the bevel of the tube was noted to be lying against the posterior tracheal wall. The tube was rotated through 90° so that the bevel of the tube pointed towards the side wall of the trachea and repeat application of the oesophageal detector device confirmed tracheal placement since the bulb now rapidly refilled.

The posterior tracheal wall is unsupported by cartilage and if the bevel of the tube is lying against the posterior wall, mucosa may be sucked into its orifice during testing with the oesophageal detector device. Rapid refilling of the bulb does not occur and oesophageal intubation is indicated erroneously.

This problem presumably only occurs when unformed tubes such as Portex or Mallinkrodt nylon reinforced tubes are used since these may rotate during insertion so that the bevel comes to lie posteriorly. The bevel will probably always point towards the side wall of the trachea when preformed tubes are used.

We strongly recommend the use of the oesophageal detector device as an aid to confirmation of tracheal placement of a tube. However, if this device indicates an 'oesophageal intubation' when other features point to tracheal placement of an unformed tube we suggest that the tube be rotated through 90° to exclude an inappropriate position of the tube bevel.

National Hospital for Nervous Disease,
Maida Vale,
London W9
I. Calder
M. Smith
M. Newton

References

1. Patil VU, Stehling LC, Zauder HL. Predicting the difficulty of intubation utilizing an intubation gauge. *Anesthesiology Review* 1983; **10:** 32–3.
2. Mallampati SR, Gatt SP, Gugino LD, Desai SP, Waraksa B, Freiberger D, Liu PL. A clinical sign to predict difficult tracheal intubation: a prospective study. *Canadian Anaesthetist's Society Journal* 1985; **32:** 429–34.

The use of a transparent mouthguard at induction

We have encountered patients who are difficult to intubate because of absent, defective or malocclusive incisor teeth. There were numerous injuries to the patient's lips, loss of teeth, chipped teeth and damaged gums, and in some cases considerable dental fees were paid to correct injury in the past. We use gauze, where indicated, to cover the teeth, or fill a gap and great care at laryngoscopy but there are nevertheless complications.

However, during the past 3 months I have acquired some transparent mouth guards, similar to the ones used by athletes (boxers and rugby players). These are put into the mouth during laryngoscopy to protect the incisors and gums. The mouth guards are transparent and one can easily visualise the entire oral cavity, posterior pharynx and larynx. There was a dramatic reduction in mouth injury in these patients and none of the patients has lost any teeth during intubation.

Nowadays patients are becoming more litigious so perhaps other practising anaesthetists might be interested in the idea because it may prove of great benefit and improve patient care.

Princess Margaret Hospital,
PO Box N3729,
Nassau,
Bahamas
G. Beneby

Another use of the pulse oximeter

A 5-week-old male infant presented to hospital with abdominal distension, constipation, pallor and dyspnoea. A provisional diagnosis of Hirschprung's disease was made and a laparotomy arranged. He looked distressed with considerable splintage of the diaphragm. He weighed 3.25 kg and was premedicated with intramuscular atropine 0.1 mg 1 hour before anaesthesia. There an intravenous infusion and a nasogastric tube was in place.

He was brought to theatre, placed on a warming mattress and, after aspiration of the nasogastric tube, an inhalation induction with nitrous oxide in oxygen and halothane was performed. His trachea was intubated with a 3.5-mm plain Portex tracheal tube and atracurium 1 mg was given. He also received two increments of pethidine 1 mg during the whole procedure which lasted just over 2 hours. His lungs were manually ventilated to normocapnia with a Jackson Rees modification of the Ayre's T-piece system with nitrous oxide in oxygen and halothane (0.5%).

The monitoring was with a continuous ECG recording, end-expired CO_2, an automatic blood pressure (Dinamap) and Biox 3700 pulse oximeter with a finger probe. Increments of atracurium (1 mg) were given up to a total of 8 mg. The oximeter showed desaturation from 96/97% to 89/92% before any movement in the patient was noticed, although muscle tone did return. Each time the muscle relaxant began to wear off the return of muscle tone and commencement of breathing resulted in some desaturation indicated by the oximeter.

We found this use of the oximeter interesting in this instance, and may be a useful adjunct to a nerve stimulator.

Derby Children's Hospital,
Derby

E.V. PILLAI
S.K. THAS

'Talking in their sleep'— a defensive practice

In view of the recent upsurge in publicity about awareness during anaesthesia and the associated potential for increased litigation, may I draw readers' attention to a recent practice I have adopted during surgical operation, particularly Caesarean section.

At some point during the operation, usually when I believe the surgical stimulus to be maximal, I state clearly to the surgeon and theatre staff that I have looked for and can find no signs to suggest that the patient is aware of the procedure.

Such a statement I believe to be valuable in the event that the patient subsequently claims to have been inadequately anaesthetised. If the patient was indeed aware during the operation, he or she should recall my statement of vigilance. This should at least reduce accusations of negligence. If the patient cannot recall my statement this may act to cast a degree of doubt on the patient's claim.

Whilst I appreciate that this practice is rather crude, and certainly not without flaw, it is a simple form of defensive medicine which surely can do no harm.

Cheltenham General Hospital,
Cheltenham,
Glos GL53 7AN

G. D. STANLEY

Subarachnoid anaesthesia with 0.25% isotonic bupivacaine for Caesarean section

During 1988, in Zimbabwe, I performed more than 200 subarachnoid blocks for Caesarean section using 0.25% bupivacaine plain. Bupivacaine 0.5% was the preferred solution until January 1988, but its supply was limited, so we had to use 0.25%.

My standard technique was to preload the circulation with 1–1.5 litres of compound sodium lactate solution. A 23 or 25-G spinal needle was used at the $L_{3/4}$ interspace with the patient sitting. Bupivacaine plain 0.25% 3.0–3.6 ml was injected over 20 seconds without barbotage. The patient was then positioned with a left lateral tilt.

The technique resulted in a block with the upper level between T_4 and T_8. The systolic blood pressure decreased below 80 mmHg in two patients, both of whom responded rapidly to fluids and ephedrine 10 mg intravenously. No patient required general anaesthesia for surgery but intravenous morphine 5–15 mg was required on five occasions.

When 0.5% bupivacaine became available again I continued to use the 0.25% solution since it seemed to be more satisfactory than 0.5%.

Poole General Hospital,
Poole BH15 2JB

A.J. WILSON

Anaesthesia, 1989, Volume 44, pages 707–711

Anaesthetic literature

This section of *Anaesthetic literature* contains references taken from *Current Contents—Life Sciences* for April 1989. The Journals which may be consulted when *Anaesthetic literature* is compiled are those listed in *Current Contents—Life Sciences*, published by the Institute of Scientific Information, Philadelphia, Pennsylvania, USA.

Abdominal surgery

Membrane site of action of CO_2 on colonic sodium absorption. Charney AN, Egnor RW. *American Journal of Physiology* 1989; **256:** (No. 3 Part 1): C584.

Reduction in index of oxygen saturation at margin of active duodenal ulcers may lead to slow healing. Leung FW, Reedy TJ *et al. Digestive Diseases and Sciences* 1989; **34:** 417.

Blood transfusion and prognosis in colerectal carcinoma. Mecklin JP, Jarvinen HJ, Ovaska JT. *Scandinavian Journal of Gastroenterology* 1989; **24:** 33.

Somatostatin—its uses in gastroenterology. Vanthiel DH *Digestive Diseases and Sciences* 1989; **34:** (Suppl): S4.

Pharmacology

Adrenergic drugs and their antagonists

Central nervous system side effects of beta-adrenergic blocking agents with high and low lipid solubility. Conant J, Engler R *et al. Journal of Cardiovascular Pharmacology* 1989; **13:** 656.

Neuropsychological side effects of beta-blockers. Dimsdale JE, Newton RP, Joist T. *Archives of Internal Medicine* 1989; **149:** 514.

Serotonergic blockade compared with beta-adrenergic blockade in systemic hypertension—a double-blind comparison of ketanserin with propranolol. Okin S, Huberfeld SI *et al. Journal of Clinical Pharmacology* 1988; **28:** 1008.

Serum noradrenaline is composed of plasma and platelet noradrenaline. Poppsnijders C, Green B, Vanderheijden E. *Annals of Clinical Biochemistry* 1989; **26** (Part 2): 191.

Beta-blockers and primary prevention of coronary heart disease in patients with high blood pressured. Psaty BM, Koepsell TD *et al. Journal of the American Medical Association* 1989; **261:** 2087.

Adenosine antagonists. Williams M. *Medicinal Research Reviews* 1989; **9:** 219.

Anaesthetic agents

Trichloroethylene cranial neuropathy—is it really a toxic neuropathy or does is activate latent herpes virus?—Hypothesis. Cavanagh JB, Buxton PH. *Journal of Neurology, Neurosurgery and Psychiatry* 1989; **52:** 297.

A benzodiazerpine receptor antagonist improves emergence of mice from halothane anaesthesia. Geller E, Schiff B *et al. Neuropharmacology* 1989; **28:** 271.

Pharmacokinetics of midazolam following intravenous and oral administration in patients with chronic liver disease and in healthy subjects. Himberg JJ, Crevoisier C. *Journal of Clinical Pharmacology* 1989; **29:** 272.

Respiratory and cardiovascular effects of thyrotropin-releasing hormone as modified by isoflurane, enflurane, pentobarbital and ketamine. Schaefer CF, Brackett DJ *et al. Regulatory Peptide* 1989; **24:** 269.

Analgesic agents

Naloxone applied to conjunctiva as a test for physical opiate dependence. Creighton FJ, Ghodse AH. *Lancet* 1989; **1:** 748.

Effects of buprenorphine on motor activity of the sphincter of Oddi in man. Cuer JC, Dapoigny M *et al. European Journal of Clinical Pharmacology* 1989; **36:** 203.

Alfentanil requirement in Crohn's disease. Increased alfentanil dose requirement in patients with Crohn's disease. Gesink-van der Veer BJG, Burm AG *et al. Anaesthesia* 1989; **44:** 209.

Role of opioid antagonists in treating intravenous cocaine abuse. Kosten TR, Kleber HD, Morgan C. *Life Sciences* 1989; **44:** 887.

Pharmacokinetics of dextromoramide in surgical patients. Pagani I, Barzaghi N *et al. Fundamental and Clinical Pharmacology* 1989; **3:** 27.

An investigation of premedication with morphine given by the buccal or intramuscular route. Simpson KH, Tring IC, Ellis FR. *British Journal of Clinical Pharmacology* 1989; **27:** 377.

Metabolic interaction between morphine and naloxone in human liver. A common pathway of glucuronidation? Wahlstrom A, Persson K, Rane A. *Drug Metabolism and Disposition: The Biological Fate of Chemicals* 1989; **17:** 218.

Muscle relaxants

Neostigmine after spontaneous recovery from neuromuscular blockade. Effect on depth of blockade monitored with train-of-four and tetanic stimuli. Goldhill DR, Wainwright AP *et al. Anaesthesia* 1989; **44:** 293.

Malignant hyperthermia—effects of halothane on the surface membrane. Laizzo PA, Lehmann-Horn F *et al. Muscle Nerve* 1989; **12:** 178.

How should residual neuromuscular blockade be detected? Miller RD. *Anesthesiology* 1989; **70:** 379.

Recovery of airway protection compared with ventilation in humans for paralysis with curare. Pavlin EG, Halle RH, Schoene RB. *Anesthesiology* 1989; **70:** 381.

Pharmacokinetics and pharmacodynamics of physostigmine in the rat after oral administration. Somani SM. *Biopharmaceutics and Drug Disposition* 1989; **10:** 187.

Other drugs

Pharmacodynamics of antibiotic penetration of tissue and surgical prophylaxis. Bergamini TM, Polk HC. *Surgery, Gynecology and Obstetrics* 1989; **168:** 283.

Binding of nonsteroidal anti-inflammatory agents and their effect on binding of racemic warfarin and its enantiomers to human serum albumin. Diana FJ, Veronich JK, Kapoor AL. *Journal of Pharmaceutical Sciences* 1989; **78:** 195.

Ranitidine for prevention of postoperative suppression of delayed hypersensitivity. Nielsen HJ, Moesgaard F, Kehlet H. *American Journal of Surgery* 1989; **157:** 291.

Influence of absorbable and nonabsorbable lipids and lipidlike substances on drug bioavailability. Roberts RJ, Leff RD. *Clinical Pharmacology and Therapeutics* 1989; **45:** 299.

Correction of blood drug levels for changes over the day. Swartz CM. *Journal of Clinical Pharmacology* 1989; **29:** 234.

Pharmacokinetic and pharmacodynamic principles of drug therapy in old age. Part I. Tsujimoto G, Hashimoto K, Hoffman BB.

The collator of this section is Dr L. Kaufman, MD, FFARCS, 145 Harley Street, London W1N 2DE. Dr Kaufman is prepared to provide on request, and at a modest charge, a new additional service to our readers. References from January 1984 have been entered on data base. The data are held on Dbase II, cpm 86 and on Dbase III, MsDos and are available on disc, together with a program providing search facilities. Enquiries direct to Dr Kaufman at the above address please.

International Journal of Clinical Pharmacology, Therapy and Toxicology 1989; **27:** 13.

Clinical pharmacokinetics in organ transplant patients. Venkataramanan R, Habucky R *et al. Clinical Pharmacokinetics* 1989; **16:** 134.

Apparatus

Catheter-induced delayed recurrent pulmonary artery hemorrhage. Carlson TA, Goldenberg IF *et al. Journal of the American Medical Association* 1989; **261:** 1943.

A Comparison of anaesthetic breathing systems during spontaneous ventilation. An *in-vitro* study using a lung model. Chan ASH, Bruce WE, Soni N. *Anaesthesia* 1989; **44:** 194.

Rebreathing during spontaneous and controlled ventilation with T-piece breathing systems: a general solution. Dorrington KL, Lehane JR. *Anaesthesia* 1989; **44:** 330.

Recording pressure at the distal end of the endotracheal tube to measure respiratory impedance. Navajas D, Farre R *et al. European Respiratory Journal* 1989; **2:** 178.

An improved technique for rapid infusion of warmed fluid using a level 1 fluid warmer. Smith JS, Snider MT. *Surgery, Gynecology and Obstetrics* 1989; **168:** 273.

Complications

Standard of care and anaesthesia liability. Cheney FW, Posner K *et al. Journal of the American Medical Association* 1989; **261:** 1599.

Epidural anaesthesia and spinal arachnoiditis. Sghirlanzoni A, Marazzi R *et al. Anaesthesia* 1989; **44:** 317.

CT demonstration of massive cerebral air embolism from pulmonary barotrauma due to cardiopulmonary resuscitation. Yamaki T, Ando S *et al. Journal of Computer Assisted Tomography* 1989; **13:** 313.

General anaesthetic procedures

Hemodynamic and metabolic changes in hepatic transplantation. Rettke SR, Janossy TA *et al. Mayo Clinic Proceedings* 1989; **64:** 232.

Anaesthesia approach to hepatic transplantation. Rettke SR, Chantigian RC *et al. Mayo Clinic Proceedings* 1989; **64:** 224.

Evaluation of preoperative hematology-coagulation screening in liver transplantation. Ritter DM, Owen CA Jr *et al. Mayo Clinic Proceedings* 1989; **64:** 216.

Cerebral effects of anaesthesia and hypothermia. Stephan H, Sonntag H *et al. Anaesthesia* 1989; **44:** 310.

General interest

Outcomes of surgery in patients 90 years of age and older. Hosking MP, Warner MA *et al. Journal of the American Medical Association* 1989; **261:** 1909.

Local analgesia

Effects of intravenous cocaine are partially attenuated by haloperidol. Sherer MA, Kumor KM, Jaffe JH. *Psychiatry Research* 1989; **27:** 117.

Spinal opioids

Opioid binding properties of the purified kappa receptor from human placenta. Ahmed MS, Zhou DH *et al. Life Sciences* 1989; **44:** 861.

Low-dose intrathecal diamorphine analgesia following major orthopaedic surgery. Reay BA, Semple AJ *et al. British Journal of Anaesthesia* 1989; **62:** 248.

Receptors for substance P and related neurokinins. Regoli D, Drapeau G *et al. Pharmacology* 1989; **38:** 1.

Intrathecal administration of 5,6-DHT or 5,7-DHT reduces morphine and substances P-antinociceptive activity in the rat. Rodrigquez FD, Rodriques RE. *Neuropeptides* 1989; **13:** 139.

Obstetric anaesthesia and analgesia

Characterization of membrane calcium channels in nonpregnant and pregnant human uterus. Batra SC, Popper LD. *Gynecologic and Obstetric Investigation* 1989; **27:** 57.

Sodium and plasma volume regulation in normal and hypertensive pregnancy: a review of physiology and clinical implications. Brown MA. *Clinical and Experimental Hypertension* 1989; **7:** 265.

Temporal patterns of cocaine use in pregnancy. Chasnoff IJ, Griffith DR *et al. Journal of the American Medical Association* 1989; **261:** 1741.

High plasma concentrations of human atrial natriuretic polypeptide in women with pregnancy-induced hypertension. Cowan BD, Martin JN Jr *et al. Clinical and Experimental Hypertension* 1988; **7:** 331.

Diurnal variations in thyrotropin, prolactin and cortisol during human pregnancy. Eriksson L, Eden S *et al. Gynecologic and Obstetric Investigation* 1989; **27:** 78.

Polyarteritis nodosa in pregnancy: a case report and brief literature review. Owen J, Hauth JC. *American Journal of Obstetrics and Gynecology* 1989; **160:** 606.

2,3-Diphosphoglycerate in normal and pathologic pregnancy: relationship to neonatal weight. Paparella P, Francesconi R *et al. American Journal of Obstetrics and Gynecology* 1989; **160:** 662.

Maternal oxygenation during normal labour. Reed PN, Colquhoun AD, Hanning CD. *British Journal of Anaesthesia* 1989; **62:** 316.

MR demonstration of reversible brain abnormalities in eclampsia. Schwaighofer W, Hesselink JR, Healy ME. *Journal of Computer Assisted Tomography* 1989; **13:** 310.

Effects of physical activity on maternal plasma beta-endorphin levels and perception of labor pain. Varrassi G, Bazzano C, Edwards WT. *American Journal of Obstetrics and Gynecology* 1989; **160:** 707.

Paediatric anaesthesia and intensive care

Factors associated with surfactant treatment response in infants with severe respiratory distress syndrome. Charon A, Taeusch HW *et al. Pediatrics* 1989; **83:** 348.

Upper airway muscle activity during nasal occlusion in newborn babies. Cohen G, Henderson-Smart DJ. *Journal of Applied Physiology* 1989; **66:** 1328.

Use of caffeine in the treatment of apnea associated with the Arnold-Chiari malformation. Davis JM, Zinman R, Aranda JV. *Developmental Pharmacology and Therapeutics* 1989; **12:** 70.

Good outcome after prolonged ventilation in an infant with cystic fibrosis. Dinwiddie R. *Journal of the Royal Society of Medicine* 1989; **82** (Suppl. 16): 44.

Classification of epileptic seizures and the epilepsies. Dreifuss FE. *Pediatric Clinics of North America* 1989; **36:** 265.

Open heart surgery in infancy. Ebert PA. *Annals of Thoracic Surgery* 1989; **47:** 321.

Nifedipine transfer into human milk. Ehrenkranz RA, Ackerman RBA, Hulse JD. *Journal of Pediatrics* 1989; **114:** 478.

Classification and analysis of fetal deaths in Massachusetts. Lammer EJ, Brown LE et al. *Journal of the American Medical Association* 1989; **261:** 1757.

Fetal acid-base status and outcome Low JA. In: Hill A, Volpe JJ, eds. *Fetal Neurology.* NY: Raven Press 1989: 195.

Temporal relationships of neuropathologic conditions caused by perinatal asphyxia. Low JA, Robertson DM, Simpson LL. *American Journal of Obstetrics and Gynecology* 1989; **160:** 608.

Pneumogram recordings in infants resuscitated for apnea of infancy. Oren J, Kelly DH, Shannon DC. *Pediatrics* 1989; **83:** 364.

Endocrine maturation and lung function in premature neonates of women with diabetes. Parker CR, Hauth JC *et al. American Journal of Obstetrics and Gynecology* 1989; **160:** 657.

Pharyngeal fluid clearance and aspiration preventive mechanisms in sleeping infants. Pickens DL, Schefft GL, Thach BT. *Journal of Applied Physiology* 1989; **66:** 1164.

Antepartum fetal monitoring—fetal movement. Rayburn WF. In: Hill A, Volpe JJ, eds. *Fetal Neurology.* NY: Raven Press 1989: 17.

Chloral hydrate sedation in neonates and infants—clinical and pharmacologic considerations. Reimche LD, Sankaran K *et al. Developmental Pharmacology* 1989; **12:** 57.

Caudal epidural morphine for control of pain following open heart surgery in children. Rosen KR, Rosen DA. *Anesthesiology* 1989; **70:** 418.

The diagnosis and treatment of fetal distress. Schifrin BS In: Hill A, Volpe JJ, eds. *Fetal Neurology.* NY: Raven Press 1989: 143.

Toxic effects of atenolol consumed during breast feeding. Schmimmel MS, Eidelman AJ *et al. Journal of Pediatrics* 1989; **114:** 476.

Catecholamines and stress in the newborn. Slotkin TA, Seidler FJ. In: Breznitz, S, Zinder O, eds. *Molecular Biology of Stress.* NY: Alan R. Liss, 1989: 133.

Drug therapy of cardiopulmonary resuscitation in children Zaritsky A. *Drugs* 1989; **37:** 356

Cardiovascular system

Physiology

Significance of hyperventilation-induced ST segment depression in patients with coronary artery disease. Ardissino D, de Servi S *et al. Journal of the American Colleges of Cardiology* 1989; **13:** 804.

Cardiopulmonary response to dynamic exercise after heart and combined heart-lung transplantation. Banner NR, Lloyd MH *et al. British Heart Journal* 1989; **61:** 215.

Water transport in red blood cell membranes. Benga G. *Progress in Biophysics and Molecular Biology* 1988: **51:** 193.

Theory of local loss of blood and fluid. Blalock A. *Clinical Orthopaedics and Related Research* 189; **240:** 3.

Atrial natriuretic peptide, an endogenous natriuretic and vasorelaxant principle for the maintenance of volume homeostasis in man. Bolli P, Muller FEB *et al.* In: Reyes AJ, Leary WP, eds. *Clinical pharmacology and therapeutic uses of diuretics.* Stuttgart: Gustav Fischer Verlag, 1988; 65.

Effects of hypoxia nad hypercapnia on atrial natriuretic factor and plasma renin activity in conscious dogs. Clozel JP, Saunier C *et al. Clinical Science* 1989; **76:** 249.

Magnesium, myocardial ischaemia and arrhythmias—the role of magnesium in myocardial infarction. Dubey A, Solomon R. *Drugs* 1989; **37:** 1.

Atrial natriuretic peptide. Espiner EA, Richards AM. *Lancet* 1989; **1:** 707.

Effect of posture on the plasma levels of atrial natriuretic factor. Franco-Saenz R, Harper D, Mulrow PJ. *Clinical and Experimental Hypertension* 1989; **11:** 337.

Cardiac and whole body (3H)noradrenaline kinetics in ischaemic heart disease contrast between unstable anginal syndromes and pacing induced ischaemia McCance AJ, Forfar JC. *British Heart Journal* 1989; **61:** 238.

Variations in the plasma concentration of atrial natriuretic factor across 24 hours. McCance DR, Roberts G *et al. Acta Endocrinologica* 1989; **120:** 266.

Cardiovascular reactivity and plasma prolactin response to mental stress in normals and hypertensives. Musumeci V, Baroni S *et al. Clinical and Experimental Hypertension* 1989; **11:** 277.

Physiologic effects of steep positioning in the surgical intensive care unit. Nelson LD, Anderson HB. *Archives of Surgery* 1989; **124:** 352.

Assessment of diastolic function of the heart: background and current applications of doppler echocardiography. Part II Clinical studies. Nishimura RA, Abel MD *et al. Mayo Clinic Proceedings* 1989; **64:** 181.

Atrial and brain natriuetic peptides share binding sites in the kidney and heart. Oehlenschlager WF, Baron DA *et al. European Journal of Pharmacology* 1989; **161:** 159.

Abnormalities in jugular venous flow velocity in pulmonary hypertension. Ranganathan N, Sivaciyan V. *American Journal of Cardiology* 1989; **63:** 719.

Macrophages, monokines, and the metabolic pathophysiology of septic shock. Saccogibson NA, Filkins JP In: Roth BL *et al.* eds. *Molecular and cellular mechanisms of septic shock.* NY: Alan R. Liss, 1989; 203.

Structure and regulation of muscarinic receptors. Schimerlik MI. *Annual Review of Physiology* 1989; **51:** 217.

Angina pectoris. Clinical characteristics, neurophysiological and molecular mechanisms. Sylven C. *Pain* 1989; **36:** 145.

Endogenous opiates and the pathogenesis of hypertension. Szilagyi JE. *Clinical and Experimental Hypertension* 1989; **11:** 1.

Blood coagulation as a part of the haemostatic system. Vandammieras MCE, Muller AD. In: Zwaal RFA, Hemker HC eds. *Blood coagulation.* Amsterdam: Elsevier, 1986: 1.

Relation of atrial natriuretic peptide release to atrial contraction. Vardas PE, Walsh KP *et al. American Journal of Cardiology* 1989; **63:** 753.

Atrial natriuretic factor. Wilkins MR, Stott RAW, Lewis HM. *Annals of Clinical Biochemistry* 1989; **26** (Part 2): 115.

Treatment and medication

Transfusion and host defenses against cancer recurrence and infection. Blumberg N, Heal JM. *Transfusion* 1989; **29:** 163.

Angiotensin-converting enzyme inhibitors in heart failure. Borek M, Charlap S, Frishman WH. *Medical Clinics of North America* 1989; **73:**; 3125.

Thrombolytic therapy. Cade JF. *Blood Reviews* 1989; **3:** 5.

The evolution of medical and surgical therapy for coronary artery disease. Califf RM, Harrell FE *et al. Journal of the American Medical Association* 1989; **261:** 2077.

The role of dopaminergic agents and the dopamine receptor in treatment for CHF. Carey RA, Jacob L. *Journal of Clinical Pharmacology* 1989; **29:** 207.

Calcium antagonists and heart failure. Charlap S, Frishman W. *Medical Clinics of North America* 1989; **73:** 339.

Beta-adrenergic blocking drugs in the treatment of congestive heart failure. Charlap S, Lichstein E, Frishman WH. *Medical Clinics of North America* 1989; **73:** 373.

Mitral valve prolapse as a risk factor for infective endocarditis. Danchin N, Voiriot P *et al. Lancet* 1989; **1:** 743.

Rapid estimation of unbound lidocaine clearance in cardiac patients-implications for reducing toxicity. Denson DD, Toltzis RJ *et al. Journal of Clinical Pharmacology* 1988; **28:** 995.

A comparison of oral milrinone, digoxin, and their combination in the treatment of patients with chronic heart failure. DiBianco R, Shabetai R *et al. New England Journal of Medicine* 1989; **320:** 677.

Pharmjacologic effects on Wy 7569: a combined calcium channel blocker and thromboxane synthetase inhibitor. Ennis C, Granger SE *et al. Journal of Cardiovascular Pharmacology* 1989; **13:** 511.

Effect of morphine on the hemodynamic and neuroendocrine responses to hemorrhage in conscious rats. Feuerstein G, Siren AL *et al. Circulatory Shock* 1989; **27:** 219.

The presentation, management and prevention of crisis in sickle cell disease in Africa. Fleming AF. *Blood Reviews* 1989; **3:** 18.

Effect of calcium channel blockers on hemodynamic responses to defibrillation. Hite PR, Schroder E *et al. American Heart Journal* 1989; **117:** 569.

Differences in cardiac responses to resuscitation from burn shock, Horton JW, Baxter CR, White DJ. *Surgery, Gynecology and Obstetrics* 1989; **168:** 201.

Blood transfusions and recurrence in head and neck cancer. Jackson RM, Rice DH. *Annals of Otology, Rhinology and Laryngology* 1989; **98:** 171.

Somatostatin analog octreotide (SMS 201–995) prevents the decrease in blood pressure after oral glucose loading in the elderly. Jansen RWMM, Peeters TL *et al. Journal of Clinical Endocrinology and Metabolism* 1989; **68:** 752.

Changing strategies in the management of heart failure. Katz AM. *Journal of the American College of Cardiology* 1989; **13:** 513.

Bronchial and cardiovascular effects of ocular topical B-antagonists in asthmatic subjects—comparison of timolol, carteolol, and metipranolol. Lejeunne CL, Hugues FC *et al. Journal of Clinical Pharmacology* 1989; **29:** 97.

The role of thrombolytic therapy in surgical practice. Moran KT, Jewell ER, Persson AV. *British Journal of Surgery* 1989; **76:** 298.

Current status of antifibrinolytic drugs. Ogston D. *Blood Reviews* 1989; **3:** 1.

Drug therapy: combined beta-adrenergic and calcium-entry blockade in angina pectoris. Packer M. *New England Journal of Medicine* 1989; **320:** 709.

Inhibition of dopamine beta-hydroxylase by captopril. Palatini P, Dabbeni-Sala F, Finotti P. *Biochemical Pharmacology* 1989; **38:** 1011.

Pathophysiology and current therapy of congestive heart failure. Parmley WW. *Journal of the American College of Cardiology* 1989; **13:** 771.

Calcium entry blockade and alpha-adrenergic vascular reactivity in human beings: differences between nicardipine and verapamil. Pedrinelli R, Taddei S, Salvedtti A. *Clinical Pharmacology and Therapeutics* 1989; **45:** 285.

Therapy with diuretics in congestive heart failure. Reyes AJ. In: Reyes AJ, Leary WP. eds. *Clinical pharmacology and therapeutic uses of diuretics*. Stuttgart: Gustav Fisher Verlag. 1988: 167.

Interaction of angiotensin converting enzyme inhibition and atrial natriuretic factor. Richards AM, Rao G *et al. Hypertension* 1989; **13:** 193.

Antihypertensive therapy in the geriatric patient. 1. A review of the role of calcium channel blockers. Riepho RW, Sowers JR. *Journal of Clincial Pharmacology* 1989; **29:** 193.

The use of inotropic agents in acute and chronic congestive heart failure. Sanders MR, Kostis JB, Frishman WH. *Medical Clinics of North America*. 1989; **73:** 283.

Pharmacological mechanisms to attenuate sympathetically induced myocardial ischemia. Schulz R, Guth BD, Heusch G. *Cardiovascular Drugs and Therapy* 1989; **3:** 43.

Hemostatic effect of tranexamic acid mouthwash in anticoagulant-treated patients undergoing oral surgery. Sindet-Pedersen S, Ramstrom G *et al. New England Journal of Medicine* 1989; **320:** 840.

The rationale for combined use of diuretics, digitalis, and vasodilators in congestive heart failure. Smith TW, Pfeffer MA. *Cardiovascular Drugs and Therapy* 1989; **3:** 13.

Renal hemodynamic consequences of angiotens in-converting enzyme inhibition in congestive heart failure. Suki WN. *Archives of Internal Medicine* 1989; **149:** 669.

Risk factors of postoperative pulmonary complications after vascular surgery. Vodinh J, Bonnet F *et al. Surgery* 1989; **105:** 360.

Calcium-antagonist receptors in the atrial tissue of patients with hypertrophic cardiomyopathy. Wagner JA, Sax FL *et al. New England Journal of Medicine* 1989; **320:** 755.

Brain tissue pH, oxygen tension, and carbon dioxide tension in profoundly hypothermic cardiopulmonary bypass. Watanabe T, Orita H *et al. Journal of Thoracic and Cardiovascular Surgery* 1989; **97:** 396.

Effect of intravenous streptokinase as compared with that of tissue plasminogen activator on left ventricular function after first MI. White HD, Rivers JT *et al. New England Journal of Medicine* 1989; **320:** 817.

Respiration

Physiology

PO_2 chemoreception in arterial chemoreceptors. Acker H. *Annual Review of Physiology* 1989; **51:** 835.

Atrial natriuretic factor in chronic obstructive lung disease with pulmonary hypertension—physiological correlates and response to peptide infusion. Adnot S, Andrivet P *et al. Journal of Clinical Investigation* 1989; **83:** 986.

Role of microvascular pressure in reactive oxygen-induced lung edema. Barnard JW, Patterson CE *et al. Journal of Applied Physiology* 1989; **66:** 1486.

Muscarinic receptor subtypes: implications for lung disease. Barnes PJ. *Thorax*. 1989; **44:** 161.

Physical characteristics of a jet in the airways. Baum M, Mutz N. *Acta Anaesthesiologica Scandinavica* 1989; **33** (Suppl. 90): 46.

Maximal expiratory and inspiratory flow-volume curves in Parkinson's disease. Bogaard J.M, Howstadt A *et al. American Review of Respiratory Disease* 1989; **139:** 610.

Transtracheal oxygen decreases inspired minute ventilation. Couser JI, Make BJ, Rassulo J. *American Review of Respiratory Disease* 1989; **139:** 627.

Review lecture. From comparative physiology of respiration to several problems of environmental adaptations and to evolution. Dejours P. *Journal of Physiology* 1989; **410:** 1.

V/Q and alveolar gas exchange in pulmonary sarcoidosis. Eklund A, Broman L *et al. European Respiratory Journal* 1989; **2:** 135.

Central venous O2 saturation and rate of arterial desaturation during obstructive apnea. Fletcher EC, Kass R *et al. Journal of Applied Physiology* 1989; **66:** 1477.

Mechanics of the respiratory system during high frequency ventilation. Freedberg JJ, Allen J *et al. Acta Anaesthesiologica Scandinavica* 1989; **33** (Suppl. 90): 39.

Response of normal subjects to inspiratory resistive unloading. Gallagher CG, Sanii R, Younes M. *Journal of Applied Physiology* 1989; **66:** 1113.

Pulmonary function in Parkinson's disease. Hovestadt A, Bogaard JM *et al. Journal of Neurology, Neurosurgery and Psychiatry* 1989; **52:** 329.

Lung function after coronary artery surgery using the internal mammary artery and the saphenous vein. Jenkins SC, Soutar SA *et al. Thorax* 1989; **44:** 209.

Ventilatory response to sustained hypoxia: effect of methysergide and verapamil. Long GR, Filuk R *et al. Respiratory Physiology* 1989; **75:** 173.

Hypercapnia and response of cerebral blood flow to hypoxia in newborn lambs. Massik J, Jones MD JR *et al. Journal of Applied Physiology* 1989; **66:** 1065.

Blunted hypoxic ventilatory drive in subjects susceptible to high-altitude pulmonary edema. Matsuzawa Y, Fujimoto K *et al. Journal of Applied Physiology* 1989; **66:** 1152.

Pulmonary and extrapulmonary contributors to hypoxemia in liver cirrhosis. Melot C, Naeije R *et al. American Review of Respiratory Disease* 1989; **138:** 632.

Mechanisms of hypoxemia in patients with status asthmaticus requiring mechanical ventilation. Rodriguezroisin R, Ballester E *et al. American Review of Respiratory Disease* 1989; **139:** 732.

Respiratory mechanics in acute quadriplegia—lung and chest wall compliance and dimensional changes during respiratory maneuvers. Scanlon PD, Loring SH *et al. American Review of Respiratory Disease* 1989; **138:** 615.

Influence of respiratory drive on upper airway resistance in normal men. Series F, Cormier Y *et al. Journal of Applied Physiology* 1989; **66,** 1242.

The response of the pulmonary circulation to exercise during normoxia and hypoxia following pneumonectomy in the adult sheep. Smith M, Coates G *et al. Canadian Journal of Physiology and Pharmacology* 1989; **67:** 202.

Ventilatory response to an inhaled constant CO_2 load and added dead space in healthy men, awake and asleep. Warley A, Clarke M *et al. Respiration Physiology* 1989; **75:** 183.

Airway mucus. Widdicombe JG. *European Respiratory Journal* 1989; **2:** 107.

Transport of oxygen in muscle. Wittenberg BA, Wittenberg JB. *Annual Review of Physiology* 1989; **51:** 857.

Treatment and medication

Superimposed high frequency ventilation with conventional mechanical ventilation. Barzilay E, Kessler D, Raz R *Chest* 1989; **95:** 681.

Humidification techniques in high-frequency ventilation—a review. Fuchs W. *A*cta Anaesthesiologia Scandinavica 1989; **33** (Suppl. 90): 120.

The effects of positive expiratory pressure on isovolume flow and dynamic hyperinflation in patients receiving mechanical ventilation. Gay PC, Rodarte JR, Hubmayr RD. *American Review of Respiratory Disease* 1989; **139:** 621.

Variations in flow and intra-alveolar pressure during jet ventilation: theoretical and experimental analysis. Guenard H, Cros AM, Boudey C. *Respiration Physiology* 1989; **75:** 235.

Electroventilation—new interest in an old idea. Jay SJ. *Chest* 1989; **95:** 487.

Proper use of aerosol corticosteroids to control asthma. Li JTC, Reed CE. *Mayo Clinic Proceedings* 1989; **64:** 205.

Supplemental oxygen and quality of sleep in patients with chronic obstructive lung disease. McKeon JL, Murree-Allen K, Saunders NA. *Thorax* 1989; **44:** 184.

Aspirin-intolerance as a precipitating factor of life-threatening attacks of asthma requiring mechanical ventilation. Picado C, Castillo JA *et al. European Respiratory Journal* 1989; **2:** 127.

The effect of inhaled naloxone on resting bronchial tone and exercise-induced asthma. Popa V, Rients P. *American Review of Respiratory Disease* 1989; **139:** 702.

Role of bronchoalveolar lavage in the diagnosis of pneumonia. Rankin JA. *Chest* 1989; **95** (Suppl.): S187.

Chest physiotherapy. Selsby DS. *British Medical Journal* 1989; **298:** 541.

Electrophrenic respiration in patients with high quadriplegia. Sharkey PC, Halter JA, Nakajima K. *Neurosurgery* 1989; **24:** 529.

Gas exchange during high frequency ventilation. Skyes MK. *Acta Anaesthesiologica Scandinavica* 1989; **33:** (Suppl. 90): 32.

Protection against pulmonary O2 toxicity by N-acetylcysteine. Wagner PD, Mathieu-Costello O *et al. European Respiratory Journal* 1989; **2:** 116.

Central nervous system

Physiology

Control of severe pain with sustained-release morphine tablets v. oral morphine solution. Arkinstall WW, Goughnour BR *et al. Canadian Medical Association Journal* 1989; **140:** 653.

Minireview: Chronic electroconvulsive shock and neurotransmitter receptors—an update. Gleiter CH, Nutt DJ. *Life Sciences* 1989; **44:** 985.

Cardiovascular and hemodynamic aspects of sleep. Laguzzi R, Nosjean A. In: Wauquier A. *et al.* eds. *Slow Wave Sleep*. NY: Raven Press, 1989: 11.

Lambert-Eaton myasthenic syndrome: immunoglobulin G inhibition of Ca2+ flux in tumor cells correlates with disease severity. Lang B, Vincent A *et al. Annals of Neurology* 1989; **25:** 265.

Steinert's disease or myotonic dystrophy, a disease unlike others. Lemieux B. *Canadian Journal of Neurological Sciences* 1989; **16:** 89.

Obstructive sleep apnea syndrome in sickle cell disease. Maddern BR, Reed HT *et al. Annals of Otology, Rhinology and Laryngology* 1989; **98:** 174.

The supraoptic nucleus: afferents from areas involved in control of body fluid homeostasis. Wilkin LD, Mitchell LD *et al. Neuroscience* 1989; **28:** 573.

Cerebrospinal fluid lactate in patients with diabetes mellitus and hypoglycaemic coma. Yao H, Sadoshima S *et al. Journal of Neurology, Neurosurgery and Psychiatry* 1989; **52:** 372.

Treatment and medication

Nimodipine reduces postischemic lactate levels in the isolated perfused rat brain. Bielenberg GW, Stierstorfer H-J *et al. Biochemical Pharmacology* 1989; **38:** 853.

Antidepressant withdrawal syndromes: phenomenology and pathophysiology. Dilsaver SC. *Acta Psychiatrica Scandinavica* 1989; **79:** 113.

The effects of ritanserin and seganserin on human slow wave sleep. Idzikowski O. In: Wauquier A, *et al.* eds. *Slow Wave Sleep*. NY: Raven Press 1989: 197.

Sleep apnea following withdrawal of amitriptyline. Musa MN. *Journal of Clinical Pharmacology* 1988; **28:** 1038.

Endocrine and metabolic

Physiology

Postoperative changes in serum creatinine: when do they occur and how much is important? Charlson ME, Mackenzie CR *et al. Annals of Surgery* 1989; **209:** 328.

Measured and predicted calorie requirements of adults during recovery from severe burn trauma. Cunningham JJ, Hegarty MT *et al. American Journal of Clinical Nutrition* 1989; **49:** 404.

Effects of arginine vasopressin on hemodynamics and lung fluid balance in lambs. Gest AL, Moise AA *et al. American Journal of Physiology* 1989; **256** (No. 3 Part 2): H641.

Arginine vasopressin potentiates natriuretic effect of atrial peptide. Graczak LM, Nicolodi LK *et al. American Journal of Physiology* 1989; **256** (No. 3 Part 2): H925.

Changes in cortical functioning with acute hypoglycemia and hyperglycemia in type-1 diabetes. Hoffman RG, Speelman DJ *et al. Diabetes Care* 1989; **12:** 193.

Brain corticotropin releasing factor and development. Insel TR, Battaglia G, Desouza EB. In: Breznitz S, Zinder O, eds. *Molecular Biology of Stress*. NY: Alan R. Liss, 1989: 19.

Lactic acidosis revisited. Johnson RN. *Annals of Clinical Biochemistry* 1989; **26** (Part 2): 113.

Examination stress, platelet peripheral benzodiazepine binding sites, and plasma hormone levels. Karp L, Weizman A *et al. Life Sciences* 1989; **44:** 1077.

Adrenergic response following recognition of stress. Kopin IJ, Eisenhoffer G, Goldstein D. In: Breznitz S, Zinder O, eds. *Molecular Biology of Stress*. NY: Alan R. Liss, 1989: 123.

Biochemistry and physiology of gastrointestinal somatostatin. Lucey MR, Yamada T. *Digestive Diseases and Sciences* 1989: **34** (Suppl.): S14.

Upper gastrointestinal involvement in diabetes mellitus: study of esophagogastric function. Pozzi M, Rivolta M *et al. Acta Diabetologica Latina* 1988: **25:** 333.

Energy expenditure in postoperative multiple organ failure with acute renal failure. Soop M, Forsberg E *et al. Clinical Nephrology* 1989; **31:** 139.

Modification of adrenergic and vasopressin receptor-linked lipid metabolism during endotoxemia. Spitzer J, Deturco EBR In: Roth BL, *et al.* eds. *Molecular and Cellular Mechanisms of Septic Shock* NY: Alan R. Liss, 1989: 77.

Opioids, stress, and the developing brain. Zagon IS, McLaughlin P. In: Breznitz S, Zinder O, eds. *molecular Biology of Stress*. NY: Alan R. Liss, 1989: 77.

Importance of cardiovascular autonomic dysfunction in IDDM subjects with diabetic nephropathy. Zander E, Schultz B *et al. Diabetes Care* 1989; **12:** 259.

Endocrine and metabolic

Treatment and medication

Medthylprednisolone pharmacokinetics after intravenous and oral administration. Al-Habet SMH, Rogers HJ. *British Journal of Clinical Pharmacology* 1989; **27:** 285.

Transferring diabetic patients to human insulin Leading Article. *Lancet* 1989; **1:** 762.

Diuretics. Levine SD. *Medical Clinics of North America* 1989; **73:** 271.

Plasma atrial natriuretic peptide and the renin-aldosterone system during long-term administration of the diuretic xipamide in man. Lijnen P, Hespel P *et al. European Journal of Clinical Pharmacology* 1989; **36:** 111.

Drug interactions with diuretics. Maharaj B. In: Reyes AJ, Leary, WP, eds. *Clinical Pharmacology and Therapeutic Uses of Diuretics*. Stuttgart: Gustav. Fisher Vedrlag, 1988: 289.

Measuring diabetic neuropathy—assessment and comparison of clinical examination and quantitative sensory testing. Maser RE, Nielsen VK *et al. Diabetes Care* 1989; **12:** 270.

Sulphonylurea antidiabetic drugs—an update of their clinical pharmacology and rational therapeutic use. Melander A, Bitzen PO *et al. Drugs* 1989; **37:** 58.

The effects of octreotide on basal and stimulated hormone levels in patients with carcinoid syndrome. Oberg K, Norheim I *et al. Journal of Clinical Endocrinology and Metabolism* 1989; **68:** 796.

Triamterene and the kidney. Sica DA, Gehr TWB. *Nephron* 1989; **51:** 454.

Pain

Physiology

Psychophysical observation on patients with neuropathic pain relieved by a sympathetic block. Price DD, Bennett GJ, Rafii A. *Pain* 1989; **36:** 273.

Treatment and medication

Treatment of severe cancer pain by low-dose continuous subcutaneous morphine. Drexel H, Dzien A *et al. Pain* 1989; **36:** 169.

Epidural steroids, epidural morphine and epidural steroids combined with morphine in the treatment of post-laminectomy syndrome. Rocco AG, Frank E *et al. Pain* 1989; **36:** 297.

Lumbar epidurography and epidural analgesia in cancer patients. Sjogren P, Gefke K *et al. Pain* 1989; **36:** 305.

Failure of epidural opioid to control cancer pain in a patient previously treated with massive doses of intravenous opioid. Tanelian DL, Cousins MJ. *Pain* 1989; **36:** 359.

Anaesthesia, 1989, Volume 44, pages 712–717

The Annual Conference of Linkmen of the Association of Anaesthetists of Great Britain and Ireland, 1988

The thirteenth Annual Conference of Linkmen was held at the Boldrewood Conference Centre, University of Southampton, on Wednesday 14 September 1988.

The President, Professor M. Rosen, was in the chair throughout the meeting. He welcomed the 207 Linkmen present, thanked them for their attendance, and expressed gratitude to Dr D. A. Saunders, Professor J. Norman and their colleagues in Southampton for making the local arrangements for the 1988 Linkmen Conference and Annual Scientific Meeting.

Professor Rosen informed Linkmen that the Association was in excellent shape; he stressed the importance of the Linkman organisation and the high value placed by Council on the information and opinions received from Linkmen. Good relations between the Association of Anaesthetists and the Faculty of Anaesthetists, RCS, ensured unity in the specialty and a strong academic base on which to build for the future. A good high public image was essential and unprofessional behaviour, such as that depicted in a recent article where an anaesthetist was reading a newspaper during anaesthesia, was thoroughly condemned.

The announcement that the College of Anaesthetists would be founded on 19 October 1988, was received with acclamation.

Efficiency in the operating theatre

In introducing the topic Dr J. E. Charlton, member of Council, said that the recent report of the Confidential Enquiry into Peri-operative Deaths and the National Audit Office publication entitled, 'The use of operating theatres in the National Health Service', have indicated that changes in the organisation of theatre services may improve the efficiency of operating theatre utilisation and lead to further improvement in standards of patient care. To respond to these reports in a positive fashion, the Association set up a working party which has met on three occasions, on one occasion with members of the Association of Surgeons.

Efficient use of operating theatres is dependent upon strong control and the working party has considered whether the appointment of a theatre services manager would be helpful. This individual would be responsible for the establisment and implementation of locally agreed guidelines for the use of operating theatres. In addition, it is recognised that data collection systems may improve theatre efficiency and the working party is keen that critical assessment and cross-benefit analysis of these systems be carried out.

The working party has also considered methods of increasing efficiency and the influence of many factors upon this process. Aspects discussed included emergency operating and the provision of emergency theatres, list organisation, multiple use of operating theatres, the anomaly of tied theatres and the use of theatres after infected cases. Factors considered likely to lead to inefficient use of theatres were late list publication, list cancellation and list overruns. Reasons for cancellation of lists and individual cases need to be investigated to ensure full utilisation of theatre resources. Consideration has also been given to staffing and training needs, admission policies and the need to match beds, patients and available resources. Finally, operating theatres can be used efficiently only when there is provision of adequate recovery facilities and support services.

A further meeting will be held with members of the Association of Surgeons in the near future with a view to publishing a joint report. The Association also intends to offer evidence to the DHSS Steering Group on the efficiency of operating departments. The recommendations of the working party will be available to Council towards the end of the year and to the membership in the middle of 1989.

Discussion. Several Linkmen including Dr K. K. Dutt (*West Birmingham*), Dr A. G. Cole (*Leicester*), Dr C. J. Barham (*East Grinstead*) and Dr R. P. Howard (*St. Helens*) participated in the discussion. The matters raised included the following: the effect of transfer of surgical services on consultants' work programmes; inefficient use of designated emergency theatres during normal working hours; alteration in published scheduled operating lists; a request for opinions on operating department computer systems; the appropriateness of Korner data for theatre audit, and reduced anaesthetic staffing levels following introduction of 'Achieving a Balance'. Dr Charlton, in reply, agreed with many of the comments and said that he would bring them to the attention of the working party.

Assistance for the anaesthetist

Dr M. M. Burrows, Honorary Treasurer and President-Elect, made reference to the necessity for adequate levels of trained assistance for anaesthetists at all times, to enhance patient safety. He said that operating department assistants (ODAs) had been singularly mismanaged for many years and he introduced the draft report of the Association working party on Assistance for the Anaesthetist. The report, drawn-up following consultation with many interested bodies, had been submitted to the DHSS Steering Group on the efficiency of operating theatres and to the NHS Training Authority. Following ratification by Council the report would be released generally and made available to members. Dr M. M. Burrows expressed gratitude to Professor M. D. Vickers, Vice-Chairman, and Dr Margaret L. Heath, Secretary, of the working party.

The main points of the report, in summary, were: (1) the safe administration of anaesthesia necessitates skilled and exclusive assistance. Anaesthetists must not tolerate the continuation of unsafe working practices, particularly if they involve trainees; (2) the current means by which help is provided for anaesthetists are failing nationally to achieve consistently acceptable numbers or quality of staff. This has already led to curtailment of elective surgery. Therefore, the problem must be solved if anaesthetic services are to be maintained; (3) assistance must be provided by staff who have been specifically trained and who have acquired relevant skills, working within a structure that promotes proper management, pay and working conditions; (4) nurse and ODA training are both adequate foundations on which such further training skills can be based; (5) proposals are described which would replace, and significantly improve, current assistance arrangements; (6) suitably qualified staff will be either anaesthetic department nurses (ADNs) or anaesthetic department assistants (ADAs); (7) the ENB Course No. 182 provides appropriate training for nurses. ADA status will be achieved by ODAs who satisfy competence-based assessment linked to the National Council for Vocational Qualifications (NCVQ).

Discussion. Dr J. S. Mason (*Mansfield*) commented on the practice of promoting ODAs to the medical physics technician, MPT, Grade IV grade. Information and advice on the extended role of ODAs was sought by Dr G. P. Clark (*Sheffield*), Dr J. H. Winder (*Southampton*) requested support from the Association to increase the grading of nurses who act as assistants for anaesthetists. In reply, Dr M. M. Burrows emphasised that nurses who acted as anaesthetists' assistants must have no other duties. He went on to say that departments of anaesthesia should agree a strategy as regards the provision of assistants locally.

The Honorary Secretary, Dr P. Morris, requested Linkmen to write to inform the Association about districts where ODAs have been upgraded to the MPT grade.

Duties of the divisional chairmen

Dr L. T. Rees (*Cardiff*), chairman of the working party on the subject explained the background to this Association initiative. Seminars held at 9, Bedford Square for chairmen of health authorities, and those for district general managers, he said, revealed that it would be helpful to both divisional chairmen and health authorities if guidelines were available on the duties of chairmen of divisions of anaesthesia and on their relationship with management. The working party had produced a report entitled 'Guidelines on duties of chairmen of divisions of anaesthesia' which was now available to the membership as an Association document.

In summary, the main recommendations of the document were: (A) Divisions of Anaesthesia will be effective only if they appear united and consultant members display a sense of corporate responsibility. (B) Health authorities should: (1) define to chairmen of divisions of anaesthesia the areas of their authority including any budgetary responsibilities; (2) define the structure of the health authority for divisional chairmen so as to identify the chain of responsibility for each clinical area and particularly which health authority officers are available, on a 24-hour, 7 day per week basis, with authority to make decisions especially in an emergency; (3) provide levels of administrative and secretarial support for divisional chairmen that enable them to discharge their duties properly. (C) Divisional chairmen should be elected and should: (1) have a maximum term of office, normally of three years; (2) accept responsibilities for advising health authorities on the efficient, safe, provision of the anaesthetic service; oversee necessary arrangements and report any deficiencies to the health authority; (3) ensure that the training programmes of trainee staff are respected; (4) ensure that all grades of anaesthetic staff are encouraged to take their full entitlement of study leave for educational purposes; (5) ensure that programmes of all anaesthetic staff are an effective use of their time and that contractual commitments are honoured; (6) ensure that records are kept of formal divisional proceedings.

Discussion. Dr K. K. Dutt (*West Birmingham*) agreed that there was a corporate responsibility but he was concerned about the conflict of opinions between individual management groups. Dr S. Srivastava (*South Tyneside*) made the comment that in small district general hospitals there was not always a separate division of anaesthesia and she requested advice on action to be taken when consultant colleagues did not satisfy their contractual commitments. The chairmen's legal responsibility for the running of the department, keeping full records and the necessity for secretarial support to enable this to be undertaken was stressed by Dr R. L. Hargrove (*Westminster*). Dr J. H. Winder (*Southampton*) asked if the dual responsibilities of clinical services manager and chairmen of division should be vested in the same individual, on account of clash of loyalties.

In reply, Dr L. T. Rees said that the obligation of consultants to satisfy their contractual commitments was mandatory; anaesthetists must keep their own house in order. It was essential that the right individuals should be encouraged to accept clinical directorships; consultation with other clinicians was important. In conclusion, Dr Rees said that the document should be sent to all chairmen of health authorities and district general managers and he encouraged Linkmen to use the document, in their interests, locally.

Standards of monitoring during anaesthesia and recovery

The President, in introducing Professor A. P. Adams, chairman of the working party on monitoring, said that monitoring influenced the practice of anaesthesia for the better. Clinical observations were paramount and should be supplemented with reasonable and comprehensive, not minimal, monitoring. Professor Adams emphasised that the practice of anaesthesia in the United Kingdom was physician-based. He stressed that if an untoward event occurred to an anaesthetised patient when the anaesthetist was absent from the operating theatre then this could be an offence under criminal rather than civil law. Monitoring, he said, comprised monitoring both the patient and the anaesthetic machine, normally on a continuous basis. The cost implications of full monitoring were not expensive. He had calculated that this was of the order of £2.00 per patient to equip fully both the anaesthetic room and operating theatre and half this amount if the patient were to be anaesthetised in the theatre as a routine practice.

The working party had produced a report, 'Recommendations for standards of monitoring during anaesthesia and recovery' which was now available to members as an Association document. The main recommendations were: (a) the anaesthetist should be present throughout the conduct of the whole anaesthetic and should ensure that an adequate record of the procedure is made; (b) monitoring should be commenced before induction of anaesthesia and continued until the patient has recovered from the anaesthetic; (c) monitoring of anaesthetic machine function should include an oxygen analyser (with alarms) and devices which enable leaks, disconnexions, rebreathing or overpressure of the system to be detected; (d) continuous monitoring of ventilation and circulation is essential. This may be performed by use of the human senses augmented, where appropriate, by the use of monitoring equipment. Clinical observations include the patient's colour, responses to the surgical stimulus, movements of the chest wall and reservoir bag, palpation of the pulse and auscultation of the breath and heart sounds. Continuous monitoring devices include the pulse plethysmograph, the pulse oximeter, the electrocardiograph, the capnograph, and devices for measuring vascular pressure and body temperature; (e). when intermittent noninvasive methods are used to measure arterial pressure and heart rate the frequency of measurement should be approximate to the clinical state of the patient; (f) a peripheral nerve stimulator should be readily available when neuromuscular blocking drugs are employed; (g) additional monitoring may be required for long or complicated operations and for patients with coexisting medical disease; (h) adequate monitoring is needed during brief anaesthetics or when using local anaesthetic or sedation techniques which may lead to loss of consciousness or to cardiovascular or respiratory complications; (i) appropriate monitoring should also be used during transport of the patient; (j) anaesthetists should issue clear instructions about monitoring postoperative care when the patient was to be supervised by recovery ward staff. Appropriate monitoring facilities should be available in the recovery ward.

Discussion. Dr M. R. Bryson (*Newcastle upon Tyne*) questioned whether anaesthetic rooms should now be phased out. Dr R. L. Hargrove (*Westminster*) strongly supported the document and said that anaesthetists would now be considered negligent if they did not monitor their patients. He recommended all anaesthetists to request their health authorities to provide the necessary monitoring equipment and, in its absence, to repeat the request every 3 months, in writing. He also stressed the importance of keeping adequate anaesthetic records and commented that there was a thin line between negligence and criminal negligence; cases had been reported to the police. Dr C. D. Hutter (*Nottingham*) was also of the opinion that anaesthetists could be deemed negligent if full monitoring was not used. Dr P. J. Bickford-Smith (*Bradford*) expressed concern about the inconsistency in the provision of equipment. Dr K. K. Dutt (*Birmingham*) was worried about equipment maintenance and calibration and suggested that anaesthetic assistants could undertake this duty. The question of the use of an anaesthetic machine pre-use checklist was raised by Dr A. M. Rollin (*Epsom*). Management had proposed this practice in her district prior to each operating session. Dr Rollin asked if use of an anaesthetic machine checklist contributed to patient safety, who should carry it out and should the anaesthetist sign that the check had been performed? Professor Adams replied that the Association had set up a working party to consider this matter and it was the intention to produce a guidance document on the subject in 1989. The anaesthetist should sign that the checklist had been completed when this was the agreed policy of the division of anaesthesia, locally. Several Linkmen were of the view that the performance of checks and full monitoring would decrease the number of operations performed per theatre session. Professor Adams again emphasised that patient safety was all important; if this meant that fewer cases could be included on a theatre list then this must be accepted by surgeons and management.

To help finance adequate monitoring equipment Dr J. F. Searle (*Exeter*) recommended Linkmen to study the apportionment of their health authority's financial resources between the acute and community sectors in their individual districts, to ensure that anaesthesia received a fair share. The President stressed that health authority budgets were large, the costs of medical legal considerations were enormous and he urged Linkmen to write to their health authorities identifying areas where substantial waste was occurring in their acute or community sectors.

Adverse drug reactions, new reporting systems

Dr W. S. Nimmo, member of Council and a member of the joint working party (Committee of Safety of Medicines, CSM, the Association of Anaesthetists and Faculty of Anaesthetists) introduced the topic and referred Linkmen to an editorial on the subject published in *Anaesthesia* 1988; **43:** 627–8 and Current Problems No. 23, September 1988, circulated to all doctors by the CSM.

In an attempt to increase the reporting of adverse reactions to anaesthetic drugs, a new yellow form had been designed specifically for anaesthetists. The aim was to make the form easier for anaesthetists to complete. A pilot scheme of the use and the success of this began on 1 September 1988 and is intended to last one year. There will be frequent review of these forms and regular reporting back to anaesthetists.

A sample form had been distributed in *Anaesthesia* and with current publications. Further supplies were available at the conference and Linkmen were asked to store some of these forms and to supply them on request to members of their divisions. It was hoped that this scheme will be supported and colleagues will be encouraged to report adverse drug reactions during anaesthesia. Generally Linkmen considered that the new forms were easier to complete. A suggestion that the new anaesthetic yellow cards should be available in the anaesthetic and recovery rooms was made by Dr Margaret L. Heath (*Lewisham*).

Intensive care services

Dr J. F. Searle, member of Council and the working party on Intensive Care Services introduced the topic and presented the results of a national survey of intensive care units, ICUs, which had been carried put by the working party with the assistance of Linkmen. In the United Kingdom, 290 general ICUs were identified; in 85% of the units an anaesthetist was in administrative charge. Dr J. F. Searle expressed gratitude to Linkmen for their invaluable assistance, without which the survey could not have been undertaken. The working party had produced a report, containing the full details of the survey, entitled 'Intensive Care Services—Provision for the Future' which was now available to the membership as an Association document.

The recommendations of the document, in summary, were: (1) records—accurate departmental records should be kept. They are essential in the evaluation of intensive care; (2) nursing staff—a nurse/patient ratio of 1 : 1 is necessary throughout the 24-hour period; (3) general intensive care units should have not less than 4 beds and admit not less than 200 patients per year; (4) location of units—one general intensive care unit should be provided in each health district. Where the workload of a district unit is less than that recommended intensive care services should be provided at a supradistrict level; (5) transfer of patients —where a hospital has no intensive care unit patients should be stabilised clinically and then transferred. The process of transfer should be the responsibility of the recipient unit; (6) consultants responsible for immediate patient care—an allocation of usually not less than 15 notional half days (NHDs) per week is required for the size of unit recommended. In 85% of units this work is done by anaesthetists. A majority of these NHDs should, therefore, be allocated to departments of anaesthesia; (7) consultant in administrative charge—each unit should have a named consultant in administrative charge.

Discussion. Dr D. F. Senior (*Dartford*), Dr A. G. Cole (*Leicester*), Dr A. L. Rawlinson (*Cuckfield*) and Dr T. B. Biswas (*Pontefract*) participated in the discussion. The matters raised included the following: difficulties in providing satisfactory training in intensive care for trainees, the optimum number of beds in an ICU; medical and nursing staff levels in ICUs; grading of nurses working in ICUs; specialised ICUs.

Dr J. F. Searle, in reply, said that trainees could be seconded for ICU experience; recommended trainee staffing levels were detailed in the document; specialised ICUs were excluded from the survey; nursing sisters in ICUs should be given the G grade; Dr M. M. Burrows, Honorary Treasurer, reiterated that specialised knowledge should be rewarded and agreed that sisters in ICUs should be graded as G.

The 'safety net'

Dr J. Edmonds-Seal, Council member, introduced the subject. He said that 'Achieving a Balance' was a tripartite agreement which was only agreed if the 'safety net' concept was accepted. The on-call rota for trainees must not be more onerous than 1:3. There was no central formula, however, guidelines were offered by the CCHMS. It was most important that arrangements were agreed by colleagues, locally. Account had to be taken of the effect of JPAC senior registrar and registrar exercises, the success or otherwise of the Overseas Doctors Training Scheme, the necessity for separate cover for obstetric and intensive care services and Faculty of Anaesthetists' requirements for training. The possibility of crossover from other specialties was limited for anaesthetists but could be arranged for some duties, for example, resuscitation, intensive care and transport of patients. Large holes could appear in the 'net' and it was important for anaesthetists to educate and train other trainees in these nonanaesthetising duties. It was not intended that the new staff grade would normally undertake on-call duties. The future of the hospital practitioner and clinical assistant grades was uncertain.

If the plans for the 'balance', to be achieved over 10 years commencing September 1988, were not fully implemented, in particular the proposed increase in consultant numbers, then the safety net would not fulfil its promise. Centralisation of acute services and rationalisation of out of hours surgery was essential. Continuing evaluation of the safety net will be most important.

Discussion. Dr M. R. Bryson (*Newcastle upon Tyne*) was concerned about increasing demands to improve services with reduced numbers of trainees. Dr J. A. Duncan (*West Fife*) was of the same opinion and predicted that additional consultant work patterns would have to change in the interests of patient safety. Professor J. Norman (*Southampton*) made the points that JPAC related to the medical profession as a whole and that JPAC's aims were to provide a good career structure for all trainee staff and an improved service to patients. Consultant anaesthetist numbers increased year by year and Professor Norman said that he did not foresee a substantial reduction in trainee staff. It was hoped that there would be an increase in the present JPAC numbers proposed for both senior registrars and registrars. Professor Norman encouraged Linkmen to be optimistic for the future; the planners' view and reality were not the same.

AIDS and the anaesthetist

The subject was introduced by Dr J. F. Searle, member of Council. Since it was first described in the summer of 1981, AIDS has become an escalating epidemic. Worldwide the number of cases continues to increase rapidly. Although, at present, the epidemic in the United Kingdom is of much smaller proportions than in the United States, it has been estimated that by the end of 1991 there will be 3 million HIV-positive individuals in this country. Council has considered three areas which are of particular concern to anaesthetists: screening for HIV, precautions against infection and the infected anaesthetist. These are discussed in detail in the Association booklet ***AIDS and Hepatitis B, guidelines for anaesthetists***, published in April 1988. The recommendations laid down in this document, together with the decisions of the July 1988, Annual Representative Meeting of the British Medical Association were summarised.

Discussion. Dr K. J. Gill (*West Dorset*) considered that the document did not differentiate satisfactorily between the guidance offered in respect to AIDS and that for Hepatitis B. He was concerned that the cost of implementing the protective measures would be considerable and urged anaesthetists, both consultants and trainees, to adopt 'clean' practices. Dr M. M. Burrows, Honorary Treasurer, commented on the legal opinions which had been obtained by various medical bodies on the necessity for consent to be obtained from the patient prior to HIV testing.

The BMA opinion was considered to be reasonable, namely that HIV testing should be performed only on clinical grounds with the specific consent of the patient. However, there might be individual clinical circumstances where a doctor believed that in the best interests of a particular patient it was necessary to depart from this rule. If the doctor did so he or she must be prepared to justify this action before the courts and the General Medical Council.

Dr P. J. Bickford-Smith (*Bradford*) requested confirmation that the anaesthetic delivery system was not an important vector in the transfer of HIV infection; this was given. Dr R. L. Hargrove (*Westminster*) was of the opinion that if HIV infection was suspected on clinical grounds then the patient should be tested. Dr J. F. Searle, in summing up, advocated the use of inexpensive, nonsterile, gloves and said that doctors must be prepared to justify testing for AIDS and this must be recognised.

Medical defence societies' subscriptions

In introducing the subject, Dr W. L. M. Baird, Assistant Honorary Secretary, said that the problem of steeply escalating medical defence association subscriptions was uppermost in the minds of all doctors. The impact of this steep rise in annual subscription has been much greater on hospital doctors since general practitioners are able to recover the cost as a legitimate practice expense. To help hospital doctors meet these costs, the 1988 Review Body Report recommended the introduction of a reimbursement scheme whereby health authorities would reimburse two thirds of the defence association subscription to whole-time hospital doctors or part-time hospital doctors who work wholly for the NHS. This recommendation has now been put into effect by the DHSS, the appropriate amendment having been made to the Terms and Conditions of Service document. The scheme, which was formulated without consultation with the profession, was intended to be an interim measure. It will apply to the period from 1 January 1988 until 31 December 1989, by which time it is anticipated that a permanent solution will have been negotiated. Anomalies both within the scheme and in its interpretation by health authorities have already been identified. Linkmen were advised to inform members to be cautious when completing health authority application forms.

The DHSS were anxious that this reimbursement scheme should not be a long-term solution. A number of other options requiring careful consideration were a no fault compensation scheme, differential indemnity rates and Crown immunity. Each option had advantages and disadvantages to individual medical specialties.

Discussion. Dr D. C. Hughes (*Surrey*) sought clarification of the position as regards the reimbursement scheme if occasionally a part-time clinical assistant anaesthetised private patients. The answer he was given was that clinical assistants should not be engaging in private practice. Dr R. L. Hargrove (*Westminster*) informed Linkmen that the Medical Defence Union, MDU, and the Medical Protection Society, MPS, normally consulted and agreed on the setting of their annual subscription rates. The MPS had recently made the decision, unilaterally, to break this arrangement and had declared their intention to introduce differential rates. There was little doubt that differential rates were a high possibility for high risk specialists. Anaesthetists were placed seventh in the MPS league of these specialties. An unanswered question was whether health authorities would pay these high rates. Dr W. L. M. Baird commented that differential subscription rates were unlikely to lead to differential salaries for consultants in high risk specialties.

Stress in trainees in anaesthesia

Dr P. J. Helliwell, Past President and Chairman of the working party on stress, introduced the topic. There was evidence of stress in trainees in general but this appeared to be more apparent in trainees in anaesthesia. Dr Helliwell made the point that although we know that stress occurs this does not mean that we condone it. From a comparison between trainees and air crews, trainees were worse off. In 1981 there were six suicides in anaesthetists in training; however, it was not possible to infer cause and effect. More recently, the results of a questionnaire to Junior Linkmen (1986) and an enquiry by the Junior Anaesthetists' Group among all registrars (1987) had brought to light a number of problems which seem to be caused by neglect of certain aspects of trainees' welfare by some departments of anaesthesia.

Dr Helliwell outlined the many factors which could induce stress. These included long hours on continuous duty, the increasing pressure of acute work in the operating theatre, ICU and on resuscitation teams, the loneliness of anaesthetists' work and the concern over the increasing incidence of litigation. Furthermore, there had been a change in social outlook. Few doctors now qualify who are not married or cohabiting. They have a home away from the hospital whereas in yesteryear the hospital was home to trainees who were, in the main, single. Nights away from base, on-call, can be ill-understood by nonmedical partners especially if the trainee has a family. This, together with the necessity for frequent moves of abode, examinations and uncertainty of career prospects undoubtedly leads to increased stress. The working party had considered these factors and had drawn up provisional recommendations for consultants to assist them in the promotion of their trainees' welfare. The working party intended to send the recommendations to the Faculty of Anaesthetists and to suggest that they be issued as a joint statement. The provisional recommendations were distributed to Linkmen and they were requested to write to the Honorary Secretary with their comments.

Discussion. Dr P. B. Taylor (*Dundee*) and Dr W. M. Ramsden (*Stoke-on-Trent*) participated in the discussion. The main issues raised were the work expected from trainees following a night or weekend on-call. Dr Helliwell considered these difficult questions to answer, particularly in regard to weekends. He said that it depended on the average on-call workload and also on the outcome of current discussions, nationally, on trainees' total weekly hours of work and maximum hours of continuous duties. This notwithstanding, Dr Helliwell strongly emphasised that trainees must have adequate rest periods to prevent fatigue from overwork which is an important contributory cause of stress in trainees. Arrangements should be flexible and be interpreted with common sense, in the best interests of patient safety.

Honorary Secretary's update

Dr P. Morris, Honorary Secretary, reported that the item published in *Anaesthesia News* under the title 'From the Honorary Secretary's Desk' would be published on a more regular basis in future, to improve communication to members about important matters considered by Council and its committees.

The programme of seminars and workshops at 9 Bedford Square had proved very popular. Acknowledgment was given to Dr J. F. Searle, Seminar Coordinating Secretary, who was retiring from this job, and Mrs Catherine Goff for all their hard work in arranging the excellent programme. During the year 22 seminars had been held, some popular ones twice, covering a wide range of topics, some suggested by members. The average attendance was 25 members making a total of just over 400 during the year.

Dr J. A. W. Wildsmith was the new Coordinating Secretary. Linkmen were encouraged to publicise and to take full advantage of the exciting seminar programme prepared for 1988/89.

The Museum at 9 Bedford Square was fully open: the current exhibition was devoted to Sir Ivan Magill. The library, specialising in historical and archival material, was being fully commissioned.

The current status of the Junior Linkman Scheme was reported and Linkmen were requested to support the endeavour to have a Junior Linkman in each health district.

Linkmen were reminded about the opportunities for postfellowship registrars to work in developing countries. A deterrent was the uncertainty of obtaining a post on return to the United Kingdom. However, a proleptic appointment could be made and Linkmen were asked to write to the Honorary Secretary if their department was willing to offer this facility.

May and Baker Pharmaceuticals Limited had consulted the Association about the probable withdrawal of the drug Ansolysen. Linkmen were requested to write to the Honorary Secretary if they considered retention of this drug was essential.

A joint meeting of the Association with the Canadian Anaesthetists' Society will be held on 9–13 June, 1989, in Ottawa. Full details of travel packages can be obtained from the Association official travel agent for the meeting, Express Boyd.

The return meeting with the Canadian Anaesthetists' Society will be held in 1993 in Scotland.

The Honorary Secretary thanked Linkmen for their support during his term of office and requested them to continue to write to his successor, Dr W. L. M. Baird, expressing their opinions on all matters of concern and interest.

Open forum

The development of a protocol to evaluate causes of major anaesthetic accidents

Dr J. Secker-Walker (*University College Hospital*) gave details of a case history, where following an anaesthetic administered by a locum, the patient failed to recover consciousness. He referred to other cases where patients were aware during anaesthesia and made the point that anaesthetic accidents did occur due to human factors. No guidelines or protocols had been drawn up to investigate these accidents unlike aircraft accidents, all of which were subject to detailed investigation. Dr Secker-Walker proposed that data should be collected about anaesthetic accidents to enable all factors, including human error, to be assessed. Support was sought for the development of an appropriate protocol.

Dr C. Maile (*Worcester*) expressed concern about locum anaesthetists and made the comment that quality control of references in respect to locums was difficult.

Remuneration for private practice

Dr K. R. Murrin (*Cardiff*) said that during recent years the recommended fees for anaesthesia had not increased in line with the increase in the provident associations' scales of fees. No support was forthcoming for the introduction of Budget BUPA in Cardiff. He asked how reasonable fees could be assured for anaesthetists and recommended separation of surgical from anaesthetic fees and that the latter should be published. Dr M. T. Inman, Chairman, Private Practice Committee, replied that the Association did produce guidelines on fees for anaesthetists in private practice, which were updated every 2 years. He also said that Budget BUPA was a national scheme, negotiated to obtain separation of the surgery and anaesthesia benefits.

Dr Margaret L. Heath (*Lewisham*) was of the opinion that a combined benefit introduced competition for payment between the surgeon and the anaesthetist.

Dr R. L. Hargrove (*Westminster*) said that he was an advisor on anaesthesia to BUPA. Surgeons and anaesthetists' fees had been separated in the past. However, this was not popular and they had been reamalgamated. The basis for the anaesthetist's fee, in 1980, was about 18% of the surgeon's fee. If the patient was adequately covered all fees would be paid. Moreover, the full fee may be claimed but BUPA will only reimburse up to the total benefit. Dr Hargrove considered that the best way forward was to stick to Association guidelines on fees and recommended anaesthetists to form groups for private practice.

The President informed Linkmen that the BUPA Charitable Foundation had established two research fellowships in anaesthesia, co-ordinated by the Association.

Discrimination at appointment interviews

Dr J. A. T. Duncan (*West Fife*) expressed the opinion that a candidate could be discriminated against on account of age at some advisory appointment committees. He said that the relevant Statutory Instrument and Circular was quite clear; the presence of a manager was entirely at the discretion of the committee. Proposed short-term contracts, of 5 years' duration, would necessitate about 4000 consultant reappointments per annum. If such a scheme was introduced then the disruptive nature of hospital, compared with general, practice would be a major disincentive to doctors wishing to opt for consultant practice in hospitals.

Other matters raised in the open forum were: anaesthesia in patients with AIDS, Analocum and time off following 24-hours on duty. Dr Srivastava (*South Tyneside*) asked whether anaesthetists could refuse to anaesthetise patients with AIDS. In reply, it was stated that to refuse to treat an AIDS patient was unethical. Dr J. H. Wright (*Tameside*) was informed that the Analocum Scheme was still operational. Dr W. N. Ramsden (*Stoke*) sought clarification about the recommended time off following 24-hours on duty. Dr M. T. Inman (*Plymouth*) stated that if trainees had been on duty for this period with less than 6 hours rest then they should not be expected for work for the next half-day.

The President, Professor M. Rosen, thanked Linkmen for their valuable and constructive comments and remarked that the 1988 meeting had the highest recorded attendance. He urged Linkmen to remain active, to keep the Linkman Coordinator, Dr J. E. Charlton, informed about changes of Linkmen and declared the meeting closed.

Anaesthesia, 1989, Volume 44, page 718

Safety Action Bulletin (89) 20

Siemens Servo ventilators, 900 Series
Attention is drawn to the fact that expiratory valves are failing some of these ventilators. Users are advised to contact the manufacturers in order to obtain replacements for these premature failures.

Seminars in Anesthesia

Editor:
RONALD L. KATZ

Editorial Board
**Richard J. Kitz, Emanuel M. Papper, John J. Bonica,
Werner Flacke and A.H. Giesecke, Jr.**

**Publication: Quarterly
Subscription: Volume 8, 1989
Institutions: £60.00 (UK)/$91.00 (Overseas)**

Seminars in Anesthesia will provide the anesthesiologist with a review of important topics in the field. Each issue will be devoted to an area of particular importance in which invited experts will discuss a wealth of clinical experience. All practising anesthesiologists will find *Seminars* a source of current and reliable information.

From a recent issue

Anesthesia for the Asthmatic Patient, *Ronald Dueck*
Thoracic Anesthesia, *Roger S. Wilson*
Anesthesia for Airway Surgery, *John V. Donlon, Jr*
Anesthesia for the Sickle Cell Diseases and Other Hemoglobinopathies, *Jeff Ray Gibson, Jr*
Anesthesia for Orthopedic Surgery, *Ralph L. Bernstein and Andrew D. Rosenberg*
Clinical Immunology of Chemonucleolysis, *Anna Uitvlugt and Jonathan Moss*
Clinical Aspects of Chemonucleolysis, *Joseph O. Reagan and Howard L. Zauder*
Anesthesia for Extracorporeal Shock Wave Lithotripsy, *David Gissen*

Coupon

Seminars in Anesthesia

*To: Journals Marketing Department
Academic Press Ltd
24–28 Oval Road
London NW1 7DX, England*

Please tick

☐ Please send me a sample copy and subscription details of *Seminars in Anesthesia*

Signature.. Name (Capitals) ....

Address ....

.... Date..........................

Contents: Anaesthesia, vol. 44, no. 8, August 1989

EDITORIAL

John Alfred Lee (1906–1989) MRCS, LRCP, MMSA, FFARCS, FFARCSI (Hon)
J. A. Lee and J. N. Lunn 631

ORIGINAL ARTICLES

Fluid deprivation before operation. The effect of a small drink
A. Agarwal, P. Chari and H. Singh 632
The effects of hypocapnic ventilation on mental function in elderly patients undergoing cataract surgery
R. M. Jhaveri 635
Anaesthesia and brain damage in the newborn
A. J. Charlton, J. M. Davies and S. Rimmer 641
Opioid supplementation during propofol anaesthesia. The effects of fentanyl or alfentanil on propofol anaesthesia in daycase surgery
A. C. Moffat, A. W. Murray and W. Fitch 644
A clinical study into the possible intrinsic bradycardic activity of vecuronium
D. A. Cozanitis and O. Erkola 648
Comparison of anxiety before induction of anaesthesia in the anaesthetic room or operating theatre
J. C. Soni and D. A. Thomas 651

CASE REPORTS

Laryngeal mask anaesthesia for repair of cleft palate
M. E. Beveridge 656
Asystole with convulsion following a subanaesthetic dose of propofol plus fentanyl
K. L. Dorrington 658
Heat stroke—an uncommon presentation
P. V. van Heerden and C. H. Collins 660
Pneumothorax caused by minitracheotomy
J. M. Silk and A. M. Marsh 663

APPARATUS

A computer-controlled anaesthetic gas mixer
R. W. Boaden, P. Hutton and C. Monk 665

HISTORICAL

A history of anaesthetic rooms
J. C. Soni and D. A. Thomas 670

SPECIAL ARTICLE

Anaesthesia and substance abuse
P. R. Wood and N. Soni 672

3 NOV 1989

FORUM

The attitudes of junior anaesthetists to research. A survey
D. G. Gaylard and J. M. Lamberty 681
Epidural anaesthesia for day care surgery. A retrospective study
V. J. Sarma and J. Lundström 683
Temazepam or midazolam for night sedation. A double-blind study
J. Irjala, J. Kanto and M. Salonen 685
Pain on injection of methohexitone. The use of lignocaine to modify pain on injection of methohexitone during anaesthesia for electroconvulsive therapy
K. H. Simpson, P. J. Halsall and C. A. Sides 688

CORRESPONDENCE 690

ANAESTHETIC LITERATURE 707

THE ANNUAL CONFERENCE OF LINKMEN OF THE ASSOCIATION OF ANAESTHETISTS OF GREAT BRITAIN AND IRELAND, 1988 712

SAFETY ACTION BULLETIN 718

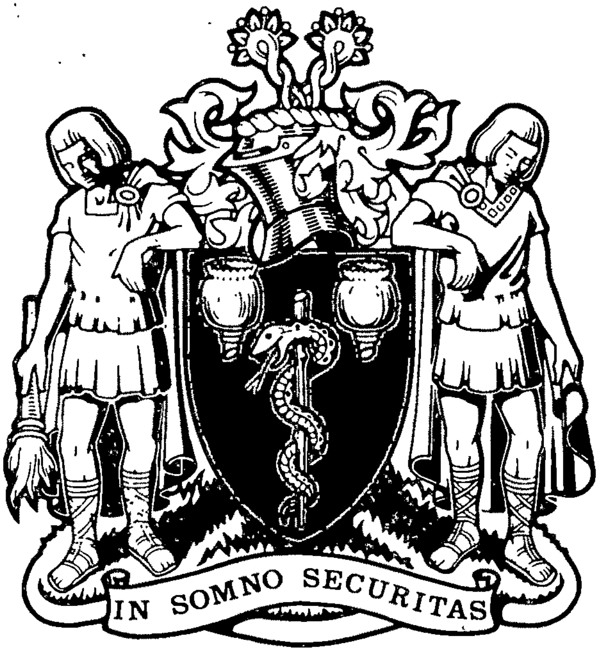
Printed by BPCC Whitefriars Ltd., Tonbridge, Kent.

5.12.90

Anaesthesia

Journal of the Association of Anaesthetists of Great Britain and Ireland

Volume 44 Number 9 September 1989



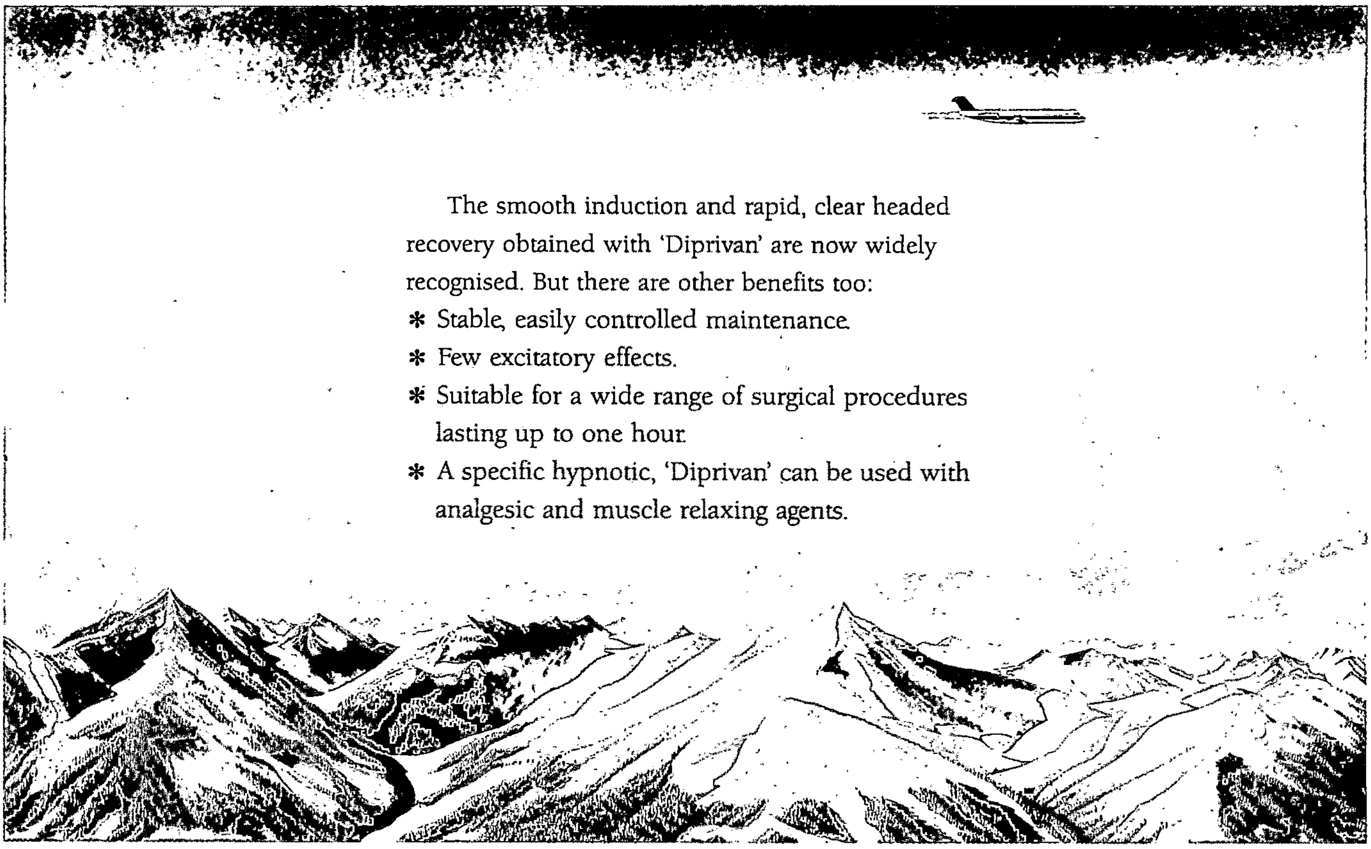
The Association of Anaesthetists of Great Britain and Ireland
Patron: HRH The Princess Margaret, Countess of Snowdon

Published for the Association by
Academic Press Grune & Stratton
London San Diego New York Boston
Sydney Tokyo Toronto

ISSN 0003-2409

If you're using 'Diprivan' for induction only,

you're not making
the most of 'Diprivan'.



The smooth induction and rapid, clear headed recovery obtained with 'Diprivan' are now widely recognised. But there are other benefits too:

* Stable, easily controlled maintenance.
* Few excitatory effects.
* Suitable for a wide range of surgical procedures lasting up to one hour.
* A specific hypnotic, 'Diprivan' can be used with analgesic and muscle relaxing agents.

▼ **'DIPRIVAN' PRESCRIBING NOTES Consult data sheet before prescribing.** Use Induction and maintenance of general anaesthesia for surgical procedures lasting up to one hour. **Presentation** Ready to use, isotonic, aqueous emulsion containing 10mg/ml propofol in a vehicle containing soybean oil and purified egg phosphatide. **Dosage and administration Induction** Titrate against response using approximately 4ml every 10 seconds in healthy adults and 2ml every 10 seconds in patients of ASA grades 3 and 4. Patients under 55 years are likely to require 2.0 to 2.5mg/kg, older patients may require approximately 20% less. **Maintenance** Usually 0.1 to 0.2mg/kg/min (6 to 12mg/kg/hr). Continuous infusion may require slightly higher rates for 10 to 20 minutes after induction. Alternatively repeat bolus injections of 25 to 50mg (2.5 to 5.0ml) may be used. **Paediatric Use** No experience in children or in mothers who are breast feeding. **Precautions:** Do not mix prior to administration with other agents or infusion fluids. Hypotension and transient apnoea may occur during induction. Occasionally, hypotension may require use of i.v. fluids and lower rate of administration during maintenance. Apply caution in cardiac, respiratory, renal or hepatic impairment; in hypovolaemic or debilitated patients; and in disorders of fat metabolism or conditions where lipid emulsions should be used cautiously. On general principles, do not use in pregnancy except for termination. **Side effects** Bradycardia responsive to atropine has been reported. Epileptiform movements have occurred rarely in temporal relationship to 'Diprivan' but no causal relationship has been established. Nausea, vomiting and headache in a small proportion of patients. Very rarely, a clinical syndrome, which may include bronchospasm and erythema accompanied by hypotension, has been reported with 'Diprivan'. Pain on injection in a proportion of patients. Venous sequelae are rare. Minimal evidence of excitation on induction. **Product licence number** 29/0190. **Basic NHS cost** £3.98 per 20ml ampoule. Lower price available for hospitals. **'Diprivan'** is a trademark.

Further information is available from: ICI Pharmaceuticals (UK), Southbank, Alderley Park, Macclesfield, Cheshire SK10 4TF.

Diprivan
propofol

ICI

Make the most of it

Anaesthesia, 1989, Volume 44, pages 719–720

Editorial

Intravenous induction agents for Caesarean section

The mother and fetus function as a unit until delivery, so that anaesthesia of the mother can induce changes which will affect them both. The baby should be born in a vigorous and healthy state after a normal delivery and the mother will be mentally and physically capable of fulfilling her maternal role in as short a time as possible. Use of general anaesthesia for Caesarean section aims to meet the normal situation as far as possible. Induction and maintenance was with inhalational agents before the advent of intravenous anaesthetics, and it was then imperative that the baby should be delivered in the shortest possible time to avoid respiratory depression from the continued transplacental passage of the anaesthetic.

Thiopentone, apart from early teething problems due to ignorance of its pharmacological effects, rapidly gained acceptance by both anaesthetists and patients. Anaesthesia could now be induced rapidly, but this was not without problems. Active vomiting was avoided, but replaced by the risk of passive regurgitation. A high concentration of thiopentone reaching the vital centres in the medulla meant that hypotension and respiratory depression were ever present possibilities. Thiopentone was introduced into obstetrics within 2 years of its first use[1] and was popularised as an induction agent for Caesarean section in the United Kingdom by Crawford.[2]

Initially, lack of knowledge of the pharmacokinetics of thiopentone in the mother at term had a marked impact on clinical practice. It was originally believed that the placenta presented a temporary barrier to the passage of thiopentone and it was recommended that the baby be delivered as soon as possible after induction to avoid any depressant effects;[3] this was practised for many years. Very short induction–delivery (I-D) times, in the region of 3 minutes, are in fact of no benefit to the fetus and may be accompanied by a high incidence of maternal awareness.[4] The placenta presents no barrier to the passage of thiopentone, and equilibration between maternal venous and cord blood occurs at about 3 minutes after induction,[5] thereafter maternal and fetal levels decline exponentially. Morgan *et al.*[6] found that the mean umbilical venous (UV) maternal venous (MV) ratio was approximately unity at the time of delivery by Caesarean section. Equilibration of thiopentone in the fetus is also a relatively rapid process, with UA to UV ratios of 0.46 with an I-D interval of 4–7 minutes[7] and 0.87 between 8 and 22 minutes.[6,8] There is thus no evidence of any adverse effect on the fetus from thiopentone when the I-D interval is extended.

The pharmacokinetics in the fetus are complicated by the fact that variations in placental blood flow affect placental drug transfer. Administration of a drug intravenously at the beginning of a uterine contraction reduces the amount available for placental transfer, as will any element of aortocaval occlusion. Interpretation of results can therefore be difficult. No correlation appears to exist between the Apgar score at delivery and either UV or UA blood levels of thiopentone. UV levels are not a reflection of the concentration presented to the fetal brain since this blood would be diluted by other fetal venous blood and there will also be some extraction of thiopentone by the fetal liver. UV levels of thiopentone found at delivery[6] are well below the arterial levels of 39–42 μg/ml necessary to produce anaesthesia in adults.[9] Too large a dose of thiopentone given to the mother, however, does increase the incidence of neonatal depression.[8] Differences also exist in the pharmacokinetics of thiopentone between nonpregnant women and those at term.[6] The elimination half-life is almost twice as long in the latter, due to a larger volume of distribution, clearance actually being greater in the pregnant state. The initial volume of distribution and rate of change of volume of distribution are similar in pregnant and nonpregnant subjects, and for a given dose of thiopentone initial plasma levels and rate of distribution are similar, so that there is no need to alter the induction dose for Caesarean section.

Each new intravenous anaesthetic has after an interval since its introduction been used in obstetrics. Methohexitone[10] and ketamine[11] confer no benefit on the fetus, although ketamine has been shown to be superior overall to thiopentone.[12] Induction with ketamine is accompanied by a significant increase in arterial blood pressure, making it unsuitable for use in those mothers with hypertensive disease. Diazepam[13] and midazolam[14] have also been used, but neither appears to offer any significant advantages over thiopentone, while sedative levels of diazepam were found in the neonate 2 hours after delivery. Infants born to mothers who had received midazolam for induction of anaesthesia were significantly inferior with regard to arm recoil, body temperature and general body tone compared to a thiopentone group.[15] Placental transfer of thiopentone was significantly faster than midazolam, while the elimination half-life of midazolam in the neonate was 6.3 hours compared to 14.7 hours for thiopentone.[16] Both the benzodiazepines and ketamine do not produce sleep in one arm–brain circulation and thus are not the most suitable agents for induction in subjects liable to regurgitation.

Etomidate is not a popular induction agent for Caesarean section in the UK despite favourable reports.[17] This is probably due to the high incidence of pain on injection and the involuntary muscle movements in unpremedicated patients; it also suppresses cortisol production in the neonate.[18] Althesin, the steroid anaesthetic which has now been withdrawn, offered no advantages over thiopentone. Propanidid has also been withdrawn, and although it appeared to be associated with a lower incidence of neonatal depression than thiopentone, its brevity of action resulted in a number of instances of factual recall.

Propofol, the most recently introduced intravenous anaesthetic, has been extensively investigated in the general surgical population and this issue of the journal reports two studies of its use in Caesarean section.[19,20]

0003–2409/89/090719+02 $03.00/0

© 1989 The Association of Anaesthetists of Gt Britain and Ireland

The Belfast group[19] found that in a dose of 2.0–2.5 mg/kg, propofol was an acceptable alternative to thiopentone; there was no difference in infant well-being. Arterial blood pressure was lower in the propofol group during the I-D interval. Recovery was marginally faster in those who received propofol. It readily crossed the placenta, with a mean UV/MV ratio of 0.72 at delivery. The results of the Finnish workers[20] were broadly similar. They found no differences in the haemodynamic response between the groups, although recovery was significantly faster after propofol induction. The rapid placental transfer of propofol was confirmed.

The introduction of intravenous induction of anaesthesia initially contributed to patients' acceptability of general anaesthesia for Caesarean section. This acceptability is marred because of recent problems of maternal awareness, but there will always be a requirement for general anaesthesia. No drug has been shown to offer sufficient advantages over thiopentone in obstetric anaesthesia to warrant its replacement. However, it is nice to know that there are acceptable alternatives for the very rare occasions when thiopentone is contraindicated, and all new drugs should be thoroughly investigated as to their suitability in obstetric practice.

Hammersmith Hospital A. HOLDCROFT
London W12 0HS M. MORGAN

References

1. SOLOMONS, E. Pentothal sodium in obstetrics. *Irish Journal of Medical Science* 1936; 746–51.
2. CRAWFORD JS. Some aspects of obstetric anaesthesia. *British Journal of Anaesthesia* 1956; **28:** 146–54.
3. HELLMAN LM, SHETTLES, LB, MANAHAN CP, EASTMAN NJ. Sodium pentothal anaesthesia in obstetrics. *American Journal of Obstetrics and Gynecology* 1944; **48:** 851–60.
4. MAGNO R, SELSTAM U, KARLSSON K. Anesthesia for caesarean section II: Effects of the induction-delivery interval on the respiratory adaptation of the newborn in elective caesarean section. *Acta Anaesthesiologica Scandinavica* 1975; **19:** 250–9.
5. MCKECHNIE FB, CONVERSE JG. Placental transmission of thiopental. *American Journal of Obstetrics and Gynecology* 1955; **70:** 639–44.
6. MORGAN DJ, BLACKMAN GL, PAULL JD, WOLF LJ. Pharmacokinetics and plasma binding of thiopental II: Studies at cesarean section. *Anesthesiology* 1981; **54:** 474–80.
7. SCHAPENS P, HEYNDRICX A. Placental transfer of thiopental. *European Journal of Toxicology* 1975; **8:** 87–93.
8. KOSAKA Y, TAKAHASHI T, MARK LC. Intravenous thiobarbiturate anesthesia for cesarean section. *Anesthesiology* 1969; **31:** 489–506.
9. BECKER, KE JR. Plasma levels of thiopental necessary for anesthesia. *Anesthesiology* 1978; **49:** 192–6.
10. MORGAN M, HOLDCROFT A, WHITWAM JG. Comparison of thiopentone and methohexitone as induction agents for Caesarean section. *Anaesthesia and Intensive Care* 1980; **8:** 431–5.
11. MOORE J, MCNABB TG, DUNDEE JW. Preliminary report on ketamine in obstetrics. *British Journal of Anaesthesia* 1971; **43:** 779–82.
12. PELZ B, SINCLAIR DM. Induction agents for Caesarean section. A comparison of thiopentone and ketamine. *Anaesthesia* 1973; **28:** 37–42.
13. HARAM K, LUND T, SAGEN N, BOE OE. Comparison of thiopentone and diazepam as induction agents of anaethesia for caesarean section. *Acta Anaesthesiologica Scandinavica* 1981; **25:** 470–6.
14. BLAND BAR, LAWES EG, DUNCAN PW, WARNELL I, DOWNING JW. Comparison of midazolam and thiopental for rapid sequence anesthetic induction for elective caesarean section. *Anesthesia and Analgesia* 1987; **66:** 1165–8.
15. RAVLO O, CARL P, CRAWFORD ME, BACH V, MIKKELSEN BO, NIELSON HK. A randomized comparison between midazolam and thiopental for elective cesarean section anesthesia. *Anesthesia and Analgesia* 1989; **68:** 234–7.
16. BACH V, CARL P, RAVLO O, CRAWFORD ME, JENSEN AG, MIKKELSEN BO, CREVOISIER C, HEIZMANN P, FATTINGER K. A randomized comparison between midazolam and thiopental for elective cesarean section anesthesia: III. Placental transfer and elimination in neonates. *Anesthesia and Analgesia* 1989; **68:** 238–42.
17. DOWNING JW, BULEY RJR, BROCK-UTNE JG, HOULTON PC. Etomidate for induction of anaesthesia at Caesarean section: comparison with thiopentone. *British Journal of Anaesthesia* 1979; **51:** 135–9.
18. REDDY BK, PIZER B, BULL PT. Neonatal serum cortisol suppression by etomidate compared with thiopentone for elective caesarean section. *European Journal of Anaesthesiology* 1988; **5:** 171–6.
19. MOORE J, BILL KM, FLYNN RJ, MCKEATING KT, HOWARD PJ. A comparison between propofol and thiopentone as induction agents in obstetric anaesthesia. *Anaesthesia* 1989; **44:** 758–62.
20. VALTONEN M, KANTO J, ROSENBERG P. Comparison of propofol and thiopentone for induction of anaesthesia for elective Caesarean section. *Anaesthesia* 1989; **44:** 758–62.

Editorial notices

Anaesthesia News

Copy for *Anaesthesia News* should be sent to the Editor as and when it becomes available. It is hoped that publication will occur within 2 months of receipt.

Manuscripts must be submitted in accordance with the internationally recognised *Uniform requirements for manuscripts submitted to biochemical journals* (*British Medical Journal* 1979; **1**: 432–5). Details will be found in the Notice to Contributors to *Anaesthesia* at the end of this issue.

Anaesthesia, 1989, Volume 44, pages 721–724

Gastric aspirates after trauma in children

S. R. W. BRICKER, A. McLUCKIE AND D. A. NIGHTINGALE

Summary

The volumes and pH of gastric aspirates obtained from 110 children (aged 1–14 years) who underwent surgery for trauma were related to the duration of pre-operative starvation and to the interval between food and injury. Aspirates were larger in children fasted for 4–6 hours than in those fasted for up to 10 hours, and were larger in children injured within 2 hours of eating than in those in whom this interval was longer ($p < 0.05$). However, 19 of 39 children (49%) starved for over 8 hours had an aspirate of more than 0.4 ml/kg, as did five of 16 children (31%) injured 3 or more hours after eating. Thus, a 'safe' interval between oral intake and induction cannot be predicted. We conclude that securing the airway by prompt tracheal intubation is the safest way to manage any child who presents for emergency anaesthesia after trauma.

Key words

Anaesthesia; paediatric.
Gastrointestinal tract; gastric volume, pH.

Children who are injured shortly after eating and who then present for emergency surgery may be at particular risk of pulmonary aspiration of gastric contents. It is widely assumed both that gastric emptying is slowed in these patients, and that the interval between last oral intake and injury has greater relevance than that between last intake and induction of anaesthesia. These assumptions, however, have not been tested formally.

This study aimed to gain information about gastric volumes after trauma in children, and to define the population of patients at greatest risk of pulmonary aspiration of gastric contents.

Methods

One hundred and ten children aged between 1 and 14 years were admitted to the study which received prior approval from the Hospital Ethics Committee. These were consecutive patients who sustained injury to the limbs or face. Children with burns or scalds, and those in whom a facial or scalp injury was associated with intracerebral trauma, were not included. Patients who required intra-oral or body cavity surgery were also excluded, as were children taking medication known to modify gastric emptying and children with any history of gastrointestinal disease.

The times of injury and of last oral intake were obtained from the patient or parent at the visit beforehand. The assessment of the accuracy of these times was necessarily subjective. However, many children were injured at play after a meal eaten at a regular time, and there was often more than one parent or teacher to corroborate the information. Children were excluded from the study if there was any uncertainty. Injuries were categorised as minor (e.g. small laceration) moderate (e.g. fractured radius and ulna) or major (e.g. fractured femur).

Patients were given analgesia as appropriate (pethidine 1 mg/kg or morphine 250 μg/kg to a maximum of 10 mg) but received no other premedication. Children were asked if they were hungry before induction of anaesthesia. A rapid sequence induction (pre-oxygenation in children who could cooperate; thiopentone 5 mg/kg; cricoid pressure; suxamethonium 1 mg/kg and tracheal intubation) was used in every case. Anaesthesia was maintained with nitrous oxide in oxygen 30%, intravenous morphine 100 μg/kg in children who had received no analgesia, atropine 20 μg/kg and either atracurium or intermittent suxamethonium to allow intermittent positive pressure ventilation throughout surgery.

The pharynx was examined at laryngoscopy for secretions. If present, these were aspirated by syringe and a fine-bore tracheal suction catheter; the pH of this fluid was measured later. Immediately after tracheal intubation, the stomach was emptied via a multi-orifice gastric tube, using gentle aspiration with a large syringe. The gastric tube

---

S.R.W. Bricker, MB, ChB, FFARCS, A. McLuckie, MB, BS, FFARCS, Registrars in Paediatric Anaesthesia, D.A. Nightingale, MB, BChir, FFARCS, Consultant Paediatric Anaesthetist, Royal Liverpool Children's Hospital, Alder Hey, Eaton Road, Liverpool L12 2AP.

Accepted 20 March 1989.

0003–2409/89/090721+04 $03.00/0

© 1989 The Association of Anaesthetists of Gt Britain and Ireland

Table 1. Gastric aspirates in injured children in relation to duration of pre-anaesthetic fasting.

	<4 hours (*n*=7)		4–6 hours (*n*=32)		6–8 hours (*n*=32)		8–10 hours (*n*=25)		>10 hours (*n*=14)		Total (*n*=110)	
Overall	Volume (ml/kg)	pH	Volume (ml/kg)	pH	Volume (ml/kg)	pH	Volume (ml/kg)	pH	Volume (ml/kg)	pH	Volume (ml/kg)	pH
Mean	1.39	1.98	1.96	2.03	1.20	1.96	0.50	1.82	1.22	1.93	1.30	1.94
Median	0.80	2.10	1.65	2.31	0.45*	2.10	0.30†	1.99*	0.45	2.00	0.60	2.16
Range	0–5.00	1.59–2.81	0–11.00	1.40–4.11	0–9.80	1.45–5.88	0–1.80	1.47–3.40	0–6.90	1.47–5.99	0–11.00	1.40–5.99

*$p<0.05$; †$p<0.001$ compared with values at 4–6 hours.

Table 2. Gastric aspirates in injured children in relation to 'last oral intake-to-injury' interval.

	0–1 hour (*n*=41)		1–2 hours (*n*=35)		2–3 hours (*n*=18)		3–4 hours (*n*=6)		>4 hours (*n*=10)		Total (*n*=110)	
Overall	Volume (ml/kg)	pH	Volume (ml/kg)	pH	Volume (ml/kg)	pH	Volume (ml/kg)	pH	Volume (ml/kg)	Volume pH	(ml/kg)	pH
Mean	2.02	1.84	1.08	1.86	0.94	2.06	0.22	1.86	0.32	2.01	1.30	1.94
Median	1.00	2.06	0.90	1.98	0.39*	2.31	0.10†	1.96	0.10‡	1.86	0.60	2.16
Range	0–11.00	1.40–5.72	0–6.90	1.47–3.82	0–3.00	1.61–5.88	0–0.60	1.65–2.17	0–1.20	1.60–5.99	0–11.00	1.40–5.99

*$p<0.05$; †$p<0.01$; ‡$p<0.005$ compared with values at 0–1 or 1–2 hours.

chosen was appropriate for the size of the child and ranged from 24 to 36 French gauge. Multiple aspirations were attempted on each patient so as to empty the stomach as completely as possible. The volume and nature of the gastric aspirates were recorded, and the pH was measured using a Pye Unicam PW 9409 digital pH meter which was calibrated before each use. The pH values were converted to hydrogen ion (H^+) concentration for statistical analysis. Gastric volumes are expressed in ml/kg body weight. It could not be assumed that gastric volumes and hydrogen ion concentrations had a normal distribution; consequently, they were analysed by the Mann–Whitney *U* test. Differences were considered to be statistically significant when $p < 0.05$.

Results

The volumes and pH of gastric aspirates are shown in Table 1. The children were allocated to groups according to the duration of pre-anaesthetic fasting (last oral intake to induction of anaesthesia): less than 4 hours, 4 to 6 hours, 6 to 8 hours, 8 to 10 hours and longer than 10 hours. Seven children were anaesthetised within 4 hours of eating or drinking because impaired circulation distal to a fracture site necessitated urgent surgical reduction. The volume of gastric contents was significantly larger in children starved for 4 to 6 hours than in those fasted for 6 to 8 hours ($p < 0.05$) or 8 to 10 hours ($p < 0.001$). There was no further decrease in volume in patients starved for longer than 10 hours. Children starved for 8 to 10 hours had gastric aspirates of significantly lower pH than those fasted for 4 to 6 hours ($p < 0.05$).

Patients were allocated also into different groups according to the interval between last oral intake and injury (Table 2). There was no difference between the median volume of gastric aspirate in children who had eaten within one hour of injury and in those who had eaten 1 to 2 hours before injury, but the aspirated volumes in both these groups were significantly larger than those in patients who had not eaten for 2 to 3 hours ($p < 0.05$), 3 to 4 hours ($p < 0.01$), or more than 4 hours ($p < 0.005$). There were no significant differences in gastric pH.

The numbers of children with a gastric aspirate of pH < 2.5, of volume > 0.4 ml/kg and of both pH < 2.5 and volume > 0.4 ml/kg are shown in Table 3. In total, 47 of 110 children (43%) had both pH < 2.5 and volume > 0.4 ml/kg, while 68 (62%) had aspirate of volume > 0.4 ml/kg. Table 4 shows the data for each of the five durations of pre-anaesthetic fasting; Table 5 shows the information for the separate intake-to-injury intervals. Data were examined from children who had received pre-operative morphine or pethidine (48 children), and those who had received neither analgesia nor any other pre-operative medication (62 children). The median time of administration of opioid was 2.0 hours pre-operatively (range 0.75 to 4.25 hours). There were no differences between these groups in volume or pH of gastric contents.

The relationship between volume of gastric contents and

Table 3. Gastric aspirates in injured children in relation to pre-operative opioid administration.

	Aspirate of pH <2.5	Aspirate of volume >0.4 ml/kg	Aspirate of pH <2.5 and volume >0.4 ml/kg
Children given opioid analgesia (*n*=48)	29 (60%)	32 (67%)	21 (44%)
Children given no premedication (*n*=62)	38 (61%)	36 (58%)	26 (42%)
Total (*n*=110)	67 (61%)	68 (62%)	47 (43%)

Table 4. Gastric aspirates in injured children in relation to duration of pre-anaesthetic fasting.

	<4 hours ($n=7$)	4–6 hours ($n=32$)	6–8 hours ($n=32$)	8–10 hours ($n=25$)	>10 hours ($n=14$)
Children with aspirate of volume >0.4 ml/kg	5 (71%)	27 (84%)	17 (53%)	11 (44%)	8 (57%)
Children with aspirate of volume >0.4 ml/kg and pH <2.5	4 (57%)	17 (53%)	10 (31%)	10 (40%)	6 (43%)

Table 5. Gastric aspirates in injured children in relation to 'last oral intake-to-injury' interval.

	<1 hour ($n=41$)	1–2 hours ($n=35$)	2–3 hours ($n=18$)	3–4 hours ($n=6$)	>4 hours ($n=10$)
Children with aspirate of volume >0.4 ml/kg	29 (71%)	27 (77%)	7 (39%)	2 (33%)	3 (30%)
Children with aspirate of volume >0.4 ml/kg and pH <2.5	20 (49%)	19 (54%)	5 (28%)	2 (33%)	0 (0%)

the degree of trauma is shown in Table 6. Volumes were significantly smaller in the minor injury group ($p < 0.05$), but there was no difference between the moderate and major injury groups. Table 7 shows the distribution of children with an aspirate of pH < 2.5 and volume > 0.4 ml/kg in relation to the severity of injury.

Forty-one of 88 children (47%) claimed to be hungry at the time of induction of anaesthesia. The technique of aspiration via an orogastric tube did not detect solid material in the stomach of 36 of these children, but solids were aspirated from the stomach of the remaining five.

Twenty-three out of 110 children (21%) vomited during emergence from anaesthesia: none vomited at induction or intra-operatively. Sixteen (26%) of the 62 patients who vomited had received no pre-operative opioid, whereas this was true of only seven (15%) of the 48 children who had required an opioid.

There was no evidence in any patient of passive regurgitation of gastric contents into the pharynx at the time of laryngoscopy.

Discussion

Pulmonary aspiration of gastric contents has been a subject of interest to anaesthetists since early studies identified it as a major factor in adult anaesthetic deaths.[1,2] Graff *et al.*[3] came to similar conclusions in their retrospective study of children published in 1964, and attributed 26% of deaths to aspiration of blood or vomit; and this work is often cited in support of the contention that aspiration is a significant cause of mortality in paediatric anaesthesia. However, there is little recent information to substantiate this. Salem *et al.*[4] undertook a retrospective study of cardiac arrest related to anaesthesia and identified only two of 73 cases as

Table 6. Volume of gastric aspirate (ml/kg) in relation to the degree of trauma.

	Minor ($n=16$)	Moderate ($n=74$)	Major ($n=20$)
Mean	0.78	1.40	1.57
Median	0.55*	0.75	1.00
Range	0–4.50	0–11.00	0–6.90

*$p<0.05$ compared with other two groups.
Minor: e.g. small laceration; moderate: e.g. fractured forearm; major: e.g. femoral fracture.

Table 7. Relation of the degree of trauma to the production of gastric aspirate of volume >0.4 ml/kg, and of volume >0.4 ml/kg and pH <2.5.

	Minor	Moderate	Major
Aspirate of volume >0.4 ml/kg ($n=68$)	10 (15%)	43 (63%)	15 (22%)
Aspirate of volume >0.4 ml/kg and pH <2.5 ($n=47$)	8 (17%)	30 (64%)	9 (19%)

Minor: e.g. small laceration; moderate: e.g. fractured forearm; major: e.g. femoral fracture.

associated with aspiration. At present, despite the many theoretical reasons why children should be more at risk than adults,[5] aspiration does not appear in practice to be a common complication. However, it can prove fatal if it does occur, and it is avoidable. Consequently, it remains important to identify children at risk, and to institute appropriate anaesthetic management in order to minimise the possibility of inhalation of gastric contents.

The pH and volume of the residual gastric secretions are considered to be of greatest significance in the patient who is fasted for elective surgery.[6–8] Severe pulmonary damage is most likely to occur if aspirated material is of pH less than 2.5 and of volume greater than 0.4 ml/kg. Particulate matter of pH as high as 5.9 has also been shown to cause extensive pulmonary damage.[9] However, it must be recognised that these data derive from experimental work in animals and should be applied to patients with caution. The gastric residual volume is clearly of importance in the patient who requires anaesthesia after a recent meal, but of equal significance may be the presence of solid material which may cause mechanical obstruction, particularly in the narrow airways of a child.

It is of concern that at least 62% of children in the present study had a volume of gastric aspirate greater than 0.4 ml/kg. This is likely to be an underestimate, as the volume retrieved was almost certainly less than the total volume; six children in whom nothing could be aspirated from the stomach subsequently vomited solids. Vomiting was common (21% of patients), but appeared to bear no direct relationship to volume of gastric aspirate, fasting time, severity of injury or the provision of analgesia. However, the value of this observation is uncertain because of the methods used in the study. Each patient's stomach was emptied at least partly at the beginning of anaesthesia, and this may have decreased the probability of vomiting; conversely, instrumentation of the pharynx, oesophagus and stomach is likely to have increased it. Nevertheless, vomiting took place only during emergence from anaesthesia, and this reinforced the view that the most critical time in the management of these children is during extubation, which should not be performed until adequate laryngeal reflexes have returned.[5,10]

Volume of gastric aspirate did show a statistically significant decrease with time, but 19 of 39 children (49%) starved for 8 hours or longer still had a volume greater than 0.4 ml/kg. The analysis of food-to-injury interval showed a similar pattern: 56 of 76 children (74%) injured within 2 hours of eating had an aspirate volume greater than 0.4 ml/kg. This proportion decreased as the interval lengthened, but five of 16 children (31%) injured 3 or more hours after food still had gastric aspirates of volume greater than 0.4 ml/kg.

In common with Olsson and Hallen,[11] we found that the severity of trauma was an important determinant of gastric volume. Fifty-eight (85%) of the 68 children with aspirate volume greater than 0.4 ml/kg had sustained either moderate or major injury. However, it is important to note that 10 patients with relatively trivial injury had substantial volumes of gastric aspirate.

Some authors consider that if a child admits to hunger then the stomach may be presumed to be empty of solids.[10] Our results do not support this assumption; five children who claimed to be hungry were found subsequently to have solid material in the stomach, and one had a gastric aspirate volume of 6.8 ml/kg.

The results of the present study suggest that some relationship between starvation time and volume of gastric aspirate can be identified in children who present for surgery after trauma, but that there is a clearer relationship between gastric volume and the interval between ingestion of food and injury. However, these relationships are not reliable enough to allow any comment as to what constitutes a 'safe' interval between oral intake and induction of anaesthesia. In the presence of a clear surgical indication for early operation the duration of pre-operative starvation does not provide a sound anaesthetic contra-indication to surgery. We consider it mandatory to secure the airway by tracheal intubation in all children who present for surgery after trauma. Our own preference is for rapid sequence intravenous induction; others may be more comfortable with an inhalational technique. Provided that the induction of anaesthesia is smooth, details of technique are less important than the recognition that the only safe premise on which to proceed is the assumption that every child who needs a general anaesthetic after trauma may have a 'full' stomach, and is therefore at risk.

References

1. EDWARDS G, MORTON HJV, PASK EA, WYLIE WD. Deaths associated with anaesthesia: a report on 1000 cases. *Anaesthesia* 1956; **11:** 194–220.
2. DINNICK OP. Deaths associated with anaesthesia. Observations on 600 cases. *Anaesthesia* 1964; **19:** 536–56.
3. GRAFF TD, PHILLIPS OC, BENSON DW, KELLEY E. Factors in pediatric anesthesia mortality. Baltimore Anesthesia Study Committee. *Anesthesia and Analgesia* 1964; **43:** 407–14.
4. SALEM MR, BENNETT EJ, SCHWEISS JF, BARAKA A, DALAL FY, COLLINS VJ. Cardiac arrest related to anesthesia. Contributing factors in infants and children. *Journal of the American Medical Association* 1975; **233:** 238–41.
5. SALEM MR, WONG AY, COLLINS VJ. The pediatric patient with a full stomach. *Anesthesiology* 1973; **39:** 435–40.
6. WYNNE JW, MODELL JH. Respiratory aspiration of stomach contents. *Annals of Internal Medicine* 1977; **87:** 466–74.
7. GREENFIELD LJ, SINGLETON RP, MCCAFFREE DR, COALSON JJ. Pulmonary effects of experimental graded aspiration of hydrochloric acid. *Annals of Surgery* 1969; **170:** 74–86.
8. MANCHIKANTI L, KRAUS JW, EDDS SP. Cimetidine and related drugs in anesthesia. *Anesthesia and Analgesia* 1982; **61:** 595–608.
9. SCHWARTZ DJ, WYNNE JW, GIBBS CP, HOOD CI, KUCK EJ. The pulmonary consequences of aspiration of gastric contents at pH values greater than 2.5. *American Review of Respiratory Disease* 1980; **121:** 119–26.
10. GOUDSOUZIAN N. Aspiration in children: practical implications. *Anesthesiology Review* 1984; **11:** 6–16.
11. OLSSON GL, HALLEN B. Pharmacological evacuation of the stomach with metoclopramide. *Acta Anaesthesiologica Scandinavica* 1982; **26:** 417–20.

Anaesthesia, 1989, Volume 44, pages 725–729

Prediction of neurological damage after cardiopulmonary bypass surgery

Use of the cerebral function analysing monitor

M. NEVIN, A. C. F. COLCHESTER, S. ADAMS AND J. R. PEPPER

Summary

Sixty-five patients who had coronary artery graft surgery were subjected to detailed neuropsychometric assessment before operation and twice again within 7 days after operation. They were monitored continuously with a cerebral function analysing monitor during the operation. The results of the peroperative cerebral monitoring were compared on completion of the study with the neuropsychometric assessments. Seventy-six percent of the patients with a significant neuropsychometric deficit after operation also showed significant peroperative changes on the analysing monitor; the majority occurred immediately after the start of perfusion. Twenty-eight patients failed to demonstrate any evidence of neuropsychometric deficit and six (21%) of these also showed significant peroperative changes. All patients whose traces demonstrated more than one significant change during the peroperative course had a significant neuropsychometric deficit afterwards.

Key words

Brain; electroencephalography.
Complications; neurological.

The introduction of the cerebral function analysing monitor (CFAM) into clinical practice in 1979[1,2] was seen as a considerable advance[3] [over the previously available cerebral function monitor (CFM)], with regard to the identification of insults likely to result in postoperative neurological deficit after cardiopulmonary bypass surgery.[4–7]

The emphasis in the majority of these papers was centred on the prediction of discrete focal cerebral deficit (stroke). It is now widely accepted that the incidence of such catastrophic events is less than 4% of all cardiopulmonary bypass cases.[8] The peroperative recognition of such events is essential if morbidity is to be reduced, but the small numbers involved have brought into question the value of such time-intensive monitoring.

Evidence has, however, been growing in the last 5 years that a much greater percentage of patients who have bypass surgery (possibly up to 75%) may demonstrate subtle neurological changes of a more diffuse nature[9–11] after operation. These changes often present as a generalised reduction in cognitive function, which although not always immediately obvious in a busy clinical setting, may have a devastating effect on the physical and psychological well-being of both the patient and his (her) immediate family. Recent evidence suggests that while in the majority of these cases the deficit is reversible, there remains a sizable minority (up to 33%) in whom the neuropsychometric damage is still evident one year later.[12] The present study, therefore, assessed the value of the CFAM as a sole predictor of this more diffuse neuropsychometric deficit; in relation to the sensitivity (the incidence of positive CFAM traces in patients in whom a postoperative neurological deficit is found) and the specificity (the incidence of negative CFAM traces in patients without postoperative neurological deficit).

It is essential to define clearly what constitutes a 'significant CFAM change' if the incidence is to be determined, but there is no universally accepted definition. We have amalgamated for the purpose of this study the classifications of earlier workers, who performed a similar assessment of the CFM, together with some additional criteria more relevant to the increased information available on the CFAM. A significant CFAM change is therefore defined as an acute change in both amplitude and frequency distribution which is maintained for a period of longer than 3 minutes and which cannot be explained in terms of alteration in either physiological or pharmacological state.

M. Nevin,* MB, BS, FFARCS, Research Fellow, A.C.F. Colchester, MRCP, PhD, Senior Lecturer, Neurology, S. Adams BSc, Research Assistant, J.R. Pepper, FRCS, Consultant Cardiac Surgeon, Departments of Cardiothoracic Surgery and Neurological Studies, St George's Hospital, London SW17 0QT and Atkinson Morley's Hospital, London SW20 0NE.

*Present address: Senior Registrar, Department of Anaesthetics, Southampton General Hospital, Tremona Road, Southampton.

Accepted 27 February 1989.

0003–2409/89/090725+05 $03.00/0 © 1989 The Association of Anaesthetists of Gt Britain and Ireland

Method

Sixty-five patients, chosen randomly from the routine list of patients who await isolated coronary artery surgery, had detailed neurological and psychometric assessments before operation and again twice in the first week afterwards. The psychometric assessment consisted of a battery of 10 tests (Table 1) designed to examine language, speech, motor and cognitive capabilities and an estimation of both social and emotional status. The choice of the tests was made after consultation with experts. All neuropsychometric analysis was performed blindly by trained assessors and comparison with CFAM tracings was performed at the end of the study.

Tests 1 to 6 inclusive were shown previously to have both high test–retest reliability coefficients and also to be highly sensitive with regard to the diffuse cerebral deficit found after coronary artery surgery.[13] The remaining tests were previously validated for use in the assessment of cerebral deficit both in the acute phase and also as an assessment of postevent recovery.[14–16] If an individual patient's postoperative score on a particular test deteriorated significantly from the pre-operative mean cohort score for that test, then that individual was said to have failed that particular test. This was then repeated for all 10 tests.

Standardised anaesthetic and surgical protocols were applied to all patients. All patients were premedicated with papaveretum (0.3 mg/kg) and hyoscine (0.06 mg/kg); insertion of arterial and right atrial lines was done under local anaesthesia after sedation with diazepam (0.15 mg/kg); induction of anaesthesia was with thiopentone (4–5 mg/kg); and maintenance of anaesthesia with an opiate and relaxant supplemented with halothane 0.5%. The surgical technique included intermittent ischaemic arrest, whole body cooling to 32°C, the use of a bubble oxygenator primed with 2 litres Ringer-lactate solution, and anticoagulation with heparin (3 mg/kg).

All patients had the routine monitoring currently accepted as standard practice at this institution (continuous monitoring of mean arterial and right atrial pressures, electrocardiogram, and intermittent blood gas, electrolyte and clotting analysis as appropriate). All patients were monitored with the CFAM for the whole duration of the operation. The scalp electrodes were sited as soon as the patient entered the anaesthetic room and the recording started shortly afterwards. We obtained a direct tracing of cerebral activity, as provided on the heat-sensitive paper in the CFAM machine, and a permanent record via a connexion to a compatible digital cassette recorder (Cristie CS6). This enabled computerised assessment of the timing of amplitude and frequency changes in relation to other intra-operative events.

Table 1. Neuropsychometric deficit.

Psychometric analysis
1. Halstead Reitan trail-making, Part A
2. Halstead Reitan trail-making, Part B

Wechsler memory scale
3. Mental control
4. Digits total
5. Visual reproduction
6. Associate learning

Frenchay aphasia screening test
7. Part A, Reception
8. Part B, Expression
9. Mental test score[16]
10. Activities of daily living (Frenchay and Barthel)

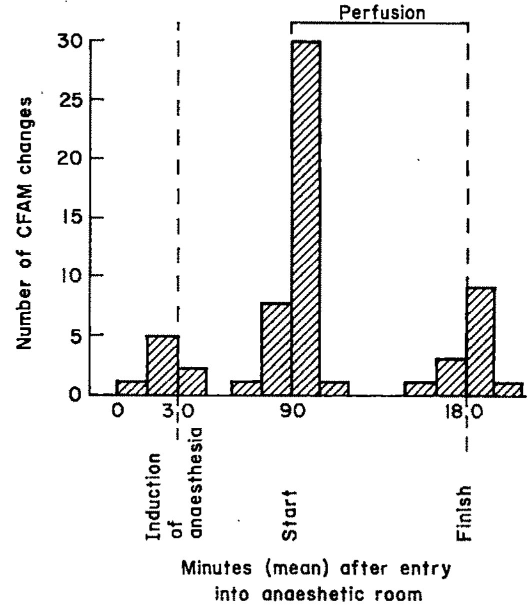


Fig. 1. Timing of peri-operative CFAM changes.

Significant changes in amplitude and frequency (as previously defined) in the CFAM signal were called positive and recorded. The characteristic findings that follow the administration of diazepam, thiopentone and hypothermia were discounted.

Results

Sixty-five patients completed the neuropsychometric assessment before operation and on the third and seventh days afterwards. All results were recorded (Table 2). It should also be noted that in some cases the postoperative score for a particular test showed an improvement over pre-operative values. The patients were then divided into three groups dependent upon their performance: a patient who failed no or one test was said to have no deficit; failure of two or three tests represented a moderate deficit; and failure of four or more tests constituted a severe deficit.

Significant CFAM changes occurred throughout the peri-operative period although examination of the timed incidence of all measured changes shows that three events were most regularly associated with abnormalities (Fig. 1).

Table 2. Neuropsychometric deficit in the sample population.

Test	% impaired by >1 SD	% impaired by >2 SD	% improved by >1 SD
1	26.2	9.2	3.1
2	30.8	12.3	1.5
3	32.3	6.2	0
4	20.0	6.2	1.5
5	12.3	7.7	6.2
6	23.1	12.3	3.1
7	36.9	9.2	1.5
8	33.8	10.7	1.5
9	10.8	1.5	3.1
10	15.4	7.7	6.2

Table 3. Neuropsychometric scores before and after operation.

Test	Mean score before operation	Mean change	Range	Wilcoxon signed rank test
1	55.0	+12.2	−7–+25	$p<0.01$
2	125.0	+37.5	−12–+68	$p<0.01$
3	8.25	−1.2	−6–0	$p<0.05$
4	13.3	−0.9	−8–+2	$p<0.05$
5	10.6	−0.4	−9–+8	$p<0.01$
6	14.6	−1.9	−11–+8	$p<0.01$
7	12.4	−4.7	−8–+1	$p<0.001$
8	13.3	−4.3	−9–+2	$p<0.005$
9	8.9	−2.4	−9–+3	$p<0.05$
10	64.7	−7.2	−25–+12	$p<0.05$

A significant proportion of patients (31%) showed more than one CFAM change during the peri-operative period. Table 3 shows the relationship between the incidence of CFAM changes and the incidence of deficit after operation.

Table 4 shows the incidence in the study population of true positives (a positive CFAM trace in a patient with postoperative deficit); and also of both false positives (a positive CFAM trace without postoperative deficit) and false negatives (a negative CFAM trace in the presence of postoperative deficit).

Discussion

The Cerebral Function Analysing Monitor (CFAM) produces a detailed analysis of the electroencephalogram and utilises both the amplitude and frequency of cerebral electrical activity as recorded from biparietal electrodes applied to the scalp. The positioning of the electrodes is critical[1] and great efforts were made throughout this study to reproduce identical scalp placement. Previous studies have identified characteristic CFAM changes associated with both the administration of drugs and also with variations in physiological variables such as temperature,[15,16] and we have not included these in this study.

We have been able to demonstrate two types of CFAM abnormalities which, in a high percentage of participants, appear to be closely linked with a demonstrable deficit after operation. The first of these changes (Fig. 2) is a sudden reduction in amplitude, associated with a reduction in fast wave activity (beta and alpha) and a simultaneous switch to a slow wave pattern (theta and delta). This was probably the most sinister CFAM change that we regularly found and in most cases was associated with dramatic alterations in cerebral perfusion pressure (mean arterial–cerebral venous pressure). A significant postoperative neuropsychometric deficit was always found in cases where these changes persisted for longer than 5 minutes, or when the return to pre-insult amplitude and frequencies was incomplete after 10 minutes.

Secondly, we identified a small group of patients in whom there was no appreciable decrease in mean amplitude voltage but who instead showed an opening up of the amplitude envelope (i.e. an increase in 90th percentile voltage associated with a decrease in 10th percentile volt-

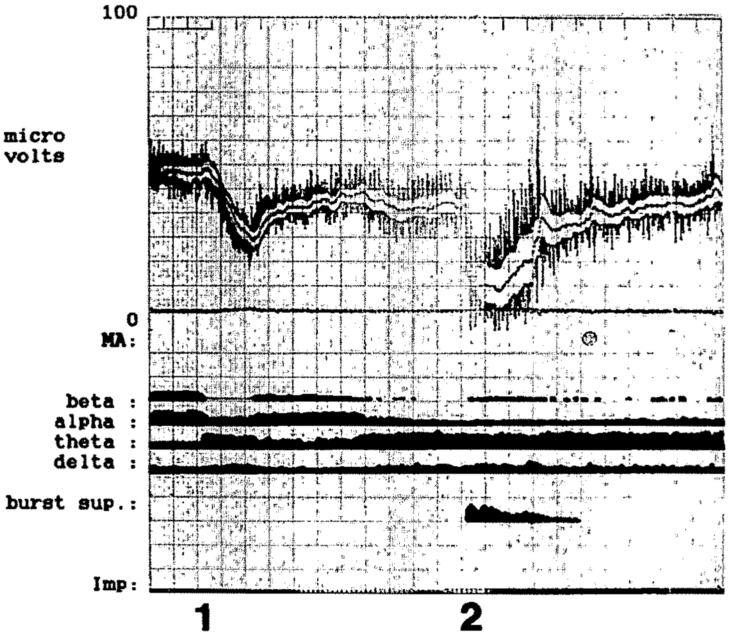


Fig. 2. Peri-operative CFAM changes—1. Reduction in amplitude and associated change to slower frequencies in a 61-year-old who had coronary artery bypass grafting. (1) Onset of perfusion (*Pa*co$_2$ 3.7 kPa); (2) sudden reduction in cerebral perfusion pressure. This patient demonstrated both a severe neuropsychometric deficit and also evidence of retinal infarction after operation.

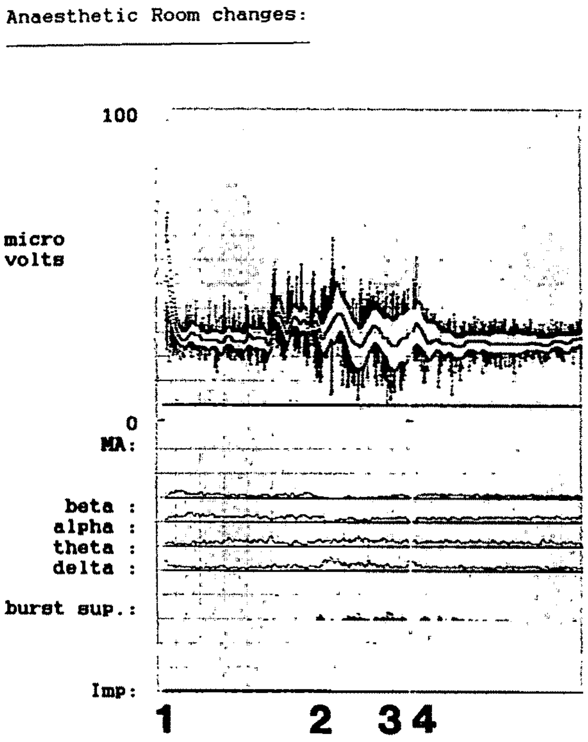


Fig. 3. Peri-operative CFAM changes—2. Opening up of amplitude envelope. The above trace was obtained from a 59-year-old patient who had coronary artery surgery. (1) Diazemuls (administered before insertion of lines under local anaesthetic); (2) the patient was placed head down; he was noted to be breathing shallowly and was difficult to rouse, (3) jugular bulb pressure 18 mmHg; (4) return to level position.

age), and a simultaneous increase in slow wave activity (Fig. 3). This change was not always associated with a postoperative neuropsychometric deficit if it occurred in isolation, but the additional presence of one of the first type of changes always resulted in a severe deficit.

Few authors have described CFAM changes which occur before the patient goes onto bypass. It is true that the majority of the abnormalities which we report occurred, as with other reports,[5] at the beginning of bypass, but there were also a significant number at other times throughout the operation.

The majority of patients who have coronary artery surgery have some limitation of cardiac performance, so it should not be surprising that any event likely to test cardiac reserve may result in a degree of cerebral hypoperfusion and the associated CFAM abnormalities. This is even more likely to be significant if other physiological abnormalities associated with cerebral hypoperfusion are also present (e.g. arterial hypocapnia).

The results of this study serve to illustrate two significant points. Firstly, it is important to have the CFAM running throughout the operation, including the period in the anaesthetic room before the induction of anaesthesia; and secondly, that several subcritical insults may be just as damaging as a single catastrophic event. All patients with two or three CFAM changes during the course of their operation were found to have significant postoperative deficit.

The finding of such a high incidence of positive CFAM traces in the patients who later showed evidence of deficit suggests that the CFAM is likely to provide a practised observer with an excellent chance of identifying cerebral insults as they occur (Table 5). The somewhat high incidence of false positives (21%) may possibly be due to an oversensitive definition of what constitutes a significant CFAM change; but is more likely to be explained by the concept of cerebral ischaemic thresholds.[19,20]

It is well recognised that as cerebral blood flow is reduced, a progressive pattern of stepwise electrophysiological changes takes place, (a reduction in the EEG to an isoelectric trace together with a reduction in both visual evoked, and finally somatosensory evoked, potentials) before permanent cerebral damage occurs. The whole value of this concept is that continuous monitoring of reliable and meaningful variables allows the recognition of a cerebral insult before recovery is impossible and the correction of the likely causes. False positives may therefore represent

Table 4. Comparison of the incidence of neuropsychometric deficit with the frequency of individual CFAM changes.

Number of CFAM changes	0	1	2	3
Neuropsychometric deficit				
None ($n=28$)	22	6	0	0
Moderate ($n=22$)	3	9	10	0
Severe ($n=15$)	2	3	7	3
% with postoperative deficit	18	67	100	100

Table 5.

The incidence of a positive CFAM in a patient with a postoperative deficit	=76%
False positives (positive CFAM/no deficit) = 6/28	=21%
False negatives (negative CFAM/+ve deficit) = 5/37	=14%

members of the cohort whose cerebral integrity was threatened by episodes of hypoperfusion, but in whom reduction in flow did not decrease to levels which would result in deficit.

These results suggest that, in the absence of any readily available method of direct measurement of cerebral oxygenation, the CFAM offers a significant improvement over previously available apparatus. It is, however, not infallible, and may need to be combined with another index of cerebral wellbeing before we have the conviction to intervene at an early stage whenever CFAM changes occur. If this degree of specificity could be achieved then the regular use of the CFAM would be associated with a significant reduction in postoperative neuropsychometric deficit.

Acknowledgment

This study was supported by a grant from the Chest Heart and Stroke Association. Considerable thanks must also be expressed towards the Department of Anaesthetics at St Georges Hospital, London.

References

1. Maynard DE. The cerebral function analyser monitor (CFAM). *Electroencephalography and Clinical Neurophysiology* 1977; **43:** (No. E115).
2. Maynard DE. Development of the CFM: The cerebral function analysing monitor (CFAM). *Annales de l'anesthesiologie française* 1979; **20:** 253–5.
3. Bolsin SNC. Detection of neurological damage during cardiopulmonary bypass. *Anaesthesia* 1986; **41:** 61–6.
4. Branthwaite MA. Factors affecting cerebral activity during open-heart surgery. *Anaesthesia* 1973; **28:** 619–25.
5. Branthwaite MA. Detection of neurological damage during open-heart surgery. *Thorax* 1973; **28:** 464–72.
6. Branthwaite MA. Prevention of neurological damage during open-heart surgery. *Thorax* 1975; **30:** 258–61.
7. Schwartz MS, Colvin MP, Prior PF, Strunin L, Simpson BR, Weaver EJM, Scott DF. The cerebral function monitor. Its value in predicting the neurological outcome in patients undergoing cardiopulmonary bypass. *Anaesthesia* 1973; **28:** 611–8.
8. Treasure T. Hearts and minds: how big is the risk of coronary surgery? (Editorial). *British Journal of Hospital Medicine* 1987; **37:** 9.
9. Shaw PJ, Bates D, Cartlidge NEF, Heaviside D, Julian DG, Shaw DA. Early neurological complications of coronary artery bypass surgery. *British Medical Journal* 1985; **291:** 1384–7.
10. Smith PLC, Treasure T, Newman SP, Joseph P, Ell PJ, Schneidau A, Harrison MJG. Cerebral consequences of cardiopulmonary bypass. *Lancet* 1986; **i:** 823–5.
11. Nevin M, Colchester ACF, Adams S, Pepper JR. Evidence for the involvement of hypocapnia and hypoperfusion in aetiology of neurological deficit after cardiopulmonary bypass. *Lancet* 1987; **ii:** 1493–5.
12. Smith PLC. The cerebral complications of coronary artery bypass surgery. *Annals of the Royal College of Surgeons of England* 1988; **70:** 212–6.
13. Shaw PJ, Bates D, Cartlidge NEF, French JM, Heaviside D, Julian DG, Shaw DA. Early intellectual dysfunction following coronary bypass surgery. *Quarterly Journal of Medicine* 1986; **225:** 59–68.
14. Wade DT, Langton Hewer R, Skilbeck CE, David RM. Assessment of stoke patients. In: *Stroke: a critical approach to diagnosis, treatment and management.* London: Chapman and Hall, 1985: 63–158.
15. Mahoney FI, Barthel DW. Functional evaluation: the Barthel index. *Maryland Medical Journal* 1965; **14:** 61–5.
16. Hodkinson HM. Evaluation of a mental test score for asessment of mental impairment in the elderly. *Age and Ageing* 1972; **1:** 233–8.
17. Frank M, Maynard DE, Tsanaclis LM, Major E, Coutinho PE. Changes in cerebral electrical activity measured by the cerebral function analysing monitor following bolus injections of thiopentone. *British Journal of Anaesthesia* 1984; **56:** 1075–81.
18. Prior PF. EEG activity and evoked potentials in brain ischaemia. *British Journal of Anaesthesia* 1985; **57:** 63–81.
19. Hinds CJ. Prevention and treatment of brain ischaemia. *British Medical Journal* 1985; **291:** 758–9.

Anaesthesia, 1989, Volume 44, pages 730–734

Propofol infusion for sedation in outpatient oral surgery

A comparison with diazepam

M. VALTONEN, M. SALONEN, H. FORSSELL, M. SCHEININ AND O. VIINAMÄKI

Summary

An infusion of propofol was compared with intravenous boluses of diazepam as sedation for minor oral surgery under local anaesthesia in 12 healthy patients who had elective bilateral surgical extraction of lower third molars; the patients served as their own controls. Plasma catecholamine, vasopressin and cortisol concentrations were determined from repeated blood samples. The total administered dose of propofol was 3.93 (SD 1.34) mg/kg and of diazepam 0.28 (SD 0.07) mg/kg. No cardiovascular depression or airway problems occurred. Other side effects were also rare but some discomfort on injection was frequent with propofol. Recovery times were faster after propofol than after diazepam as assessed by the Maddox wing and visual analogue scales. Propofol also provided better amnesia compared to diazepam at the time of the extraction of the teeth. Eight of the 12 patients subjectively preferred propofol sedation. There was no hormonal stress response in either group.

Key words

Anaesthetics, intravenous; propofol.
Hypnotics, benzodiazepines; diazepam.

Fear and anxiety about pain are common reasons for patients to delay dental care. Fear, apprehension, anaesthesia and surgery are also accompanied by various and often harmful cardiovascular, metabolic and hormonal responses.[1-3] Sedation in combination with local anaesthesia has been used as a safe alternative to general anaesthesia for the control of peri-operative pain and anxiety in oral surgery.[4-6] Spontaneous respiration, protective reflexes and the patient's cooperation are retained with an optimal degree of sedation, while the harmful responses to anxiety and pain are reduced, and recovery to street fitness is also rapid.[6-7]

Propofol is a fast acting intravenous anaesthetic agent with a short duration of action, rapid elimination and low incidence of excitatory effects.[8-10] It provides good control of the level of sedation with little accumulation and quick recovery when given as a continuous intravenous infusion for sedation.[11-13] This suggests that a propofol infusion could also be suitable for sedation during oral surgery.

The aim of the present study was to compare a propofol infusion with intravenous bolus administration of diazepam in outpatients who had oral surgery with the aid of local anaesthesia.

Methods

Twelve healthy ASA 1 patients who had elective surgical extraction of both lower third molars (on two occasions) were selected for the study. Their ages, weights and heights were respectively 24.4 years (SD 2.9), 66.2 kg (SD 15.5) and 168 cm (SD 8.9). The interval between the two operations was at least 2 weeks. Exclusion criteria were any drug allergy, pregnancy, concurrent acute or chronic illness and any acute or chronic drug therapy. The study was approved by the Hospital Ethics Committee and informed consent was obtained from each patient.

The patients were allocated randomly to receive either propofol or diazepam sedation on the first occasion, and were given the alternative sedative agent on their second visit; they were unaware of the sedative agent used, had fasted overnight and were unpremedicated. An intravenous cannula was introduced in the left antecubital fossa. Propofol was administered by slow infusion with an infusion pump at an initial rate of 10 mg/minute, titrated to slurring of speech or ptosis. Thereafter the infusion rate was adjusted according to the clinical response with a maximum rate of 6 mg/kg/hour. Diazepam (as Diazemuls)

M. Valtonen, MD, Resident in Anaesthesiology, M. Salonen, MD, Staff Anaesthetist, Department of Anaesthesiology, H. Forssell, DDS, PhD, Senior Lecturer of Dentistry, Department of Dentistry, M. Scheinin, MD, Senior Lecturer of Pharmacology, O. Viinamäki, MSc, Research Associate, Department of Pharmacology, University of Turku, Turku University Hospital, Turku, Finland.

Accepted 15 February 1989.

0003–2409/89/090730+05 $03.00/0

© 1989 The Association of Anaesthetists of Gt Britain and Ireland

was injected at a rate of 5 mg/minute and titrated analogously. The local anaesthetic used was 2 ml prilocaine (30 mg/ml) with felypressin (0.54 μg/ml).

Systolic and diastolic arterial pressures were recorded by an automated indirect sphygmomanometer with printout at 5-minute intervals. Arterial oxygen saturation (Sa_{O_2}) and plethysmographic pulse were measured indirectly with a finger probe and continuously with a pulse oximeter. The ECG was monitored throughout.

The presence of any side effects during or after sedation, especially airway problems, was noted. The duration of the operations was recorded. The dental surgeon assessed the degree of difficulty of surgery from 0 to 10 (0, easy, 10, difficult) and graded the patient's cooperation (0, poor, 10, excellent). Completeness of recovery was monitored with assessments of the critical flicker fusion threshold[14] and the Maddox wing,[15] and subjective sedation of the patients was measured with a visual analogue scale (VAS).[16] These measurements were made before the administration of the sedative agent (baseline, B) and at 15, 30, 60 and 120 minutes after the end of surgery.

Amnesia was assessed by testing the patients' recall of events during and after sedation. These included insertion of the intravenous cannula, administration of the sedative agent and the local anaesthetic, extraction of the tooth, recovery room care and the journey home. These questions were asked on a visit a week after each operation. The patients were also asked to give their subjective preference of the two sedation procedures.

Venous blood samples were collected for determination of plasma adrenaline, noradrenaline, vasopressin and cortisol. The following time points were used when the samples were collected: before the start of sedation, after a rest period of 15 minutes from the time of insertion of the intravenous cannula (0); when the end-point of sedation was achieved; 15 minutes after the start of surgery; 180 minutes after induction of sedation. The samples were collected into precooled test tubes that contained EDTA, and immediately transported at 0°C to the laboratory, where they were centrifuged and stored at −70°C until analysis. Plasma catecholamines were determined using high performance liquid chromatography (HPLC).[17] The intra-assay coefficients of variation were 2% at > 0.5 nmol, and approximately 10% at 0.1 nmol for adrenaline and noradrenaline. Plasma AVP was measured with radioimmunoassay (RIA) without previous extraction,[18] modified with sequential saturation.[19] The intra-assay coefficient of variation was about 7%. Concentrations of cortisol in plasma were determined using commercially available radioimmunoassay kits with intra-assay coefficients of variation below 5%.

Table 1. Induction characteristics, duration of operation, and assessments by dental surgeon of difficulty of operation and patient cooperation, mean (SD).

	Propofol (n = 12)	Diazepam (n = 12)
Induction time, minutes	4.33 (2.23)	4.20 (1.95)
Induction dose, mg/kg	1.04 (0.57)	0.28 (0.07)
Maintenance dose, mg/kg	2.89 (0.77)	— —
Total dose, mg/kg	3.93 (1.34)	0.28 (0.07)
Duration of operation, minutes	27.9 (12.1)	26.6 (10.2)
Difficulty of operation, 0–10	4.58 (2.56)	4.61 (2.52)
Patient cooperation, 0–10	9.51 (0.22)	9.51 (0.24)

Table 2. Analysis of variance (two-way ANOVA on repeated measures on two factors): effects of drug (propofol/diazepam) and time.

		Factor 1: drug	Factor 2: time	Interaction: drug × time
Heart rate	F	19.79	2.01	5.05
	p	0.001	0.076	0.0004
Systolic blood pressure	F	8.15	1.55	1.39
	p	0.015	0.17	0.23
Diastolic blood pressure	F	5.98	1.57	2.73
	p	0.032	0.16	0.021
Plethysmographic amplitude	F	4.11	16.4	3.57
	p	0.067	<0.0001	0.045
Noradrenaline	F	3.84	12.4	2.22
	p	0.08	<0.0001	0.10
Adrenaline	F	0.003	4.83	1.79
	p	0.95	0.006	0.16
Vasopressin	F	0.500	3.12	1.80
	p	0.49	0.038	0.16
Cortisol	F	0.047	58.30	0.55
	p	0.83	<0.0001	0.65
Maddox	F	3.81	13.3	2.00
	p	0.078	<0.0001	0.11
VAS	F	2.04	17.65	2.41
	p	0.18	<0.0001	0.064
CFF	F	0.45	6.83	1.67
	p	0.52	0.0002	0.17

Data are presented as mean (SD). Mean arterial pressure was calculated as $\frac{1}{3} \times$ (systolic + 2 × diastolic pressures). The statistical analysis was performed using two-way ANOVA (repeated measures on two factors) followed by Duncan's multiple-range test.[20] Correlations were calculated using a linear regression program. Differences between groups were analysed with Student's *t*-test (paired data) for parametric data and Fisher's exact test for nonparametric data. A p-value of less than 0.05 was considered statistically significant.

Results

The mean induction dose for propofol was 1.04 (0.57) mg/kg and the steady state infusion rate 4.18 (1.71) mg/kg/

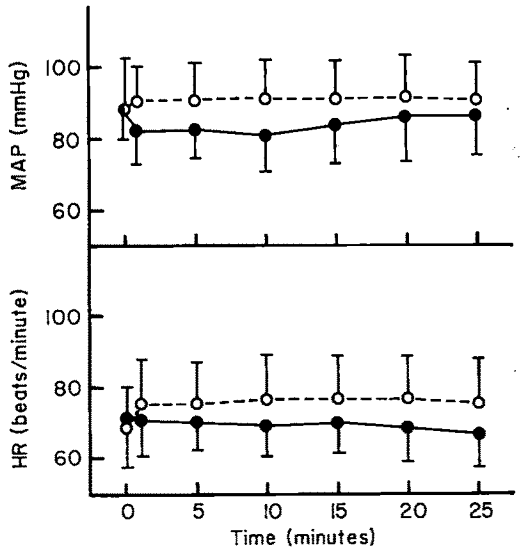


Fig. 1. Mean arterial pressure (MAP) and heart rate (HR) as a function of time after the start of sedation in propofol (●) and diazepam (○) groups (mean, SD, repeated measures ANOVA).

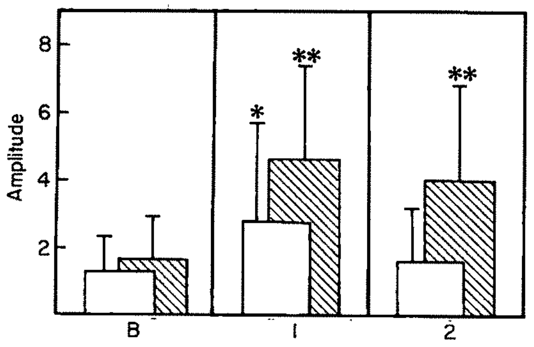


Fig. 2. Plethysmographic pulse amplitude (arbitrary units) from finger probe of pulse oximeter before sedation (B), at end-point of sedation before surgery (1) and after 15 minutes of surgery (2) in patients treated with propofol (hatched blocks) and diazepam (white blocks) [mean, SD; repeated measures ANOVA followed by Duncan's multiple-range test; * = $p < 0.05$, ** = $p < 0.01$ within groups compared with baseline (B)].

hour. The mean total dose (induction plus maintenance) for propofol was 3.93 (1.34) mg/kg. The mean induction dose of diazepam was 0.28 (0.07) mg/kg and no additional doses were needed during the operation. The induction time did not differ between propofol and diazepam (Table 1). The mean arterial pressure and heart rate values were lower throughout the procedure with propofol compared to diazepam sedation (Table 2, Fig. 1). Arterial oxygen saturation was over 95% throughout the study after both treatments. The plethysmographic pulse amplitude displayed better peripheral circulation with propofol compared to diazepam at the end-point of sedation (before surgery) and during the surgery (Table 2, Fig. 2).

The duration of the procedure was similar on both occasions and neither the difficulty of surgery nor the patient's cooperation assessed by the dental surgeon differed between the two treatments (Table 1). The side effects during and after the procedure were few, except the discomfort on injection which was a frequent finding with propofol compared to diazepam (6 versus 0, $p = 0.0069$; Table 3). No major adverse reactions occurred during or after sedation.

Recovery times were shorter after propofol than after diazepam with respect to both measurements with the Maddox wing and subjective sedation at 30 and 60 minutes after the end of the procedure (Table 2, Fig. 3). Amnesia at the time of the extraction of the tooth was more frequent with propofol compared to diazepam (9 versus 3, $p = 0.02$; Table 4). Eight patients subjectively preferred propofol sedation and four favoured diazepam.

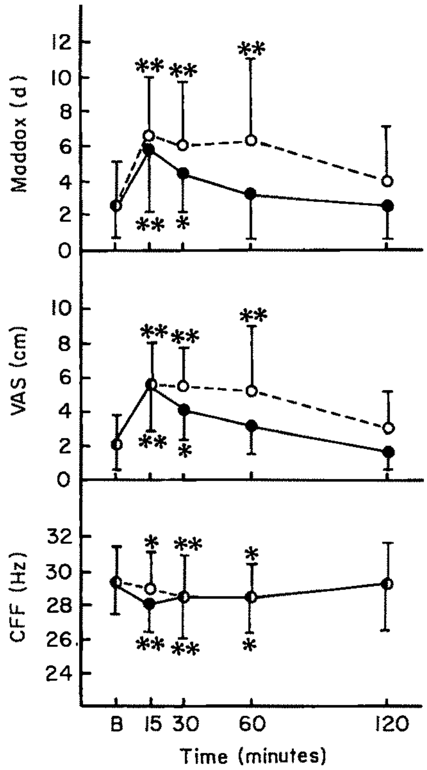


Fig. 3. Completeness of recovery assessed by Maddox wing (Maddox), visual analogue scale (VAS) and critical flicker fusion threshold (CFF) before the administration of sedative agents (B) and 15, 30, 60 and 120 minutes after the end of surgery in propofol (●) and diazepam (○) groups [mean, SD; repeated measures ANOVA followed by Duncan's multiple-range test; * = $p < 0.05$, ** = $p < 0.01$ within groups compared with baseline (B)].

Hormone responses are summarised in Table 5. Plasma adrenaline, noradrenaline and cortisol levels were similarly decreased after both sedative agents, and plasma AVP levels were also slightly decreased after propofol (Tables 2 and 5). The plethysmographic pulse amplitude and plasma noradrenaline levels showed an inverse linear relationship ($r = -0.41$, $p = 0.0002$, $n = 72$).

Discussion

Diazepam has a wide margin of safety and is commonly used for intravenous sedation in oral surgery.[21-23] However, when the degree of sedation is inadequate, additional doses

Table 3. Number of patients with side effects during and after sedation.

	Propofol	Diazepam
	($n = 12$)	
Induction		
Discomfort on injection	6	0*
Dizziness	0	2
Visual disturbances	1	0
Maintenance		
Twitching	2	0
Recovery	0	0

*$p = 0.0069$ (Fisher's exact test).

Table 4. Number of patients who recalled (on control visit) specific events during and after sedation.

	Propofol	Diazepam
	($n = 12$)	
Events		
Insertion of cannula	12	12
Induction of anaesthesia	12	12
Local anaesthesia	7	6
Extraction of tooth	3	9*
Recovery room care	12	12
Journey home	12	12

*$p = 0.020$ (Fisher's exact test).

Table 5. Venous plasma catecholamine (nmol/litre), cortisol (nmol/litre) and AVP (pg/ml) concentrations after sedation with intravenous propofol or diazepam, mean (SD). Samples: 0, baseline; I, at end-point of sedation; II, after 15 minutes of surgery; III, 180 minutes after induction. Differences between groups were not statistically significant (paired *t*-test after ANOVA). Within-group differences were analysed with Duncan's multiple-range test after ANOVA.

		Propofol		Diazepam	
		$(n=12)$			
Adrenaline (nmol/litre)	0	0.09	(0.07)	0.11	(0.07)
	I	0.06	(0.03)*	0.06	(0.04)**
	II	0.07	(0.06)	0.07	(0.06)**
	III	0.09	(0.07)	0.06	(0.04)**
Noradrenaline (nmol/litre)	0	1.85	(0.81)	1.45	(0.48)
	I	0.99	(0.48)**	0.86	(0.42)**
	II	1.02	(0.54)**	1.16	(0.60)
	III	1.75	(0.82)	1.29	(0.59)
Cortisol (nmol/litre)	0	410.0	(127.0)	403.0	(136.0)
	I	363.0	(151.0)	377.0	(121.0)
	II	299.0	(146.0)**	333.0	(149.0)*
	III	165.0	(56.0)**	149.0	(63.0)**
AVP (pg/ml)	0	6.9	(3.4)	5.8	(3.5)
	I	5.5	(3.1)**	6.2	(3.5)
	II	5.1	(2.8)**	5.6	(3.1)
	III	5.7	(2.8)*	6.2	(3.5)

$* = p<0.05$; $** = p<0.01$ [within groups compared to baseline (B) value].

of diazepam, or combinations with other drugs can cause long-lasting residual effects and prolonged recovery. Clinical studies also suggest that recovery times after equipotent doses of the rapidly eliminated benzodiazepine derivate, midazolam, are comparable to those after diazepam.[24-26]

Both diazepam and propofol produced adequate sedation during oral surgery in the present study. No clinically significant cardiovascular depression or airway problems occurred. Other side effects were also rare, but some discomfort on injection was frequent with propofol (50%).

The Maddox wing and subjective estimates of sedation showed more rapid recovery after propofol than diazepam, and the difference between the treatments was most significant 60 minutes after the end of surgery. This suggests that patients may be discharged earlier after propofol sedation than diazepam. The critical flicker fusion threshold test was less sensitive in the detection of differences between the two treatments, which is in agreement with our earlier findings.[27-29] The recovery times were shorter after propofol than after diazepam, although propofol provided better amnesia at the time of the extraction of the tooth. This may be a reason for the subjective preference of eight of the patients (67%) towards propofol. Two of the four patients who favoured diazepam assessed the propofol sedation as too potent; one complained of visual disturbances and one could not name the reason for his preference.

Direct methods to measure stress responses to pain and apprehension are lacking so measurements of stress hormone levels in blood are often used for this purpose. These measurements may be unreliable in patients with pre-existing disease; however, we included only healthy patients in this study. Our results showed that minor oral surgery under adequate intravenous sedation and local anaesthesia is associated with no stress response as assessed with plasma adrenaline, noradrenaline, cortisol and vasopressin levels. The highest values of these hormones were found before the start of sedation. Slight elevation of these baseline levels was probably caused by the pre-operative apprehension of the unpremedicated patients. The concentrations of plasma adrenaline, noradrenaline and cortisol decreased during and after the surgical procedure with both treatments. The decline of plasma cortisol was probably due to the diurnal physiological variation in the secretion of this hormone,[30] whereas the rapid decrease in the concentration of noradrenaline in blood was likely to be a reflection of the sympatholytic activity of the potent sedative agents.[31] The vasopressin levels were decreased only after propofol. One possible explanation for this may be a direct drug effect on vasopressin release. Some drugs have been reported to decrease AVP release[32] and propofol may have a similar effect. The inverse linear relationship between plasma noradrenaline and the plethysmographic pulse amplitude suggests that pulse oximetry may also give some useful semiquantitative information about changes in sympathetic neuronal activity.

In conclusion, intravenous administration of propofol or diazepam with local anaesthesia provided good sedation for oral surgery, with no hormonal stress responses. Recovery was faster after propofol compared to diazepam which may offer the advantage of earlier patient discharge. Propofol infusion appears to be an effective and safe alternative to diazepam sedation in minor oral surgery.

Acknowledgments

The authors thank ICI, Helsinki, for supplies of propofol, and Datex Co. for an opportunity to use the pulse oximeter. We also want to thank Mrs T. Ahola for assistance during this investigation.

References

1. Ryder W. The electrocardiogram in dental anaesthesia. *Anaesthesia* 1970; **25**: 46–62.
2. Goldstein DS, Dionne R, Sweet J, Gracely R, Brewer HB, Gregg R, Keiser HR. Circulatory, plasma catecholamine, cortisol, lipid, and psychological responses to a real-life stress (third molar extractions): effects of diazepam sedation and of

inclusion of epinephrine with local anesthetic. *Psychosomatic Medicine* 1982; **44:** 259–72.

3. Edmondson HD, Roscoe B, Vickers MD. Biochemical evidence of anxiety in dental patients. *British Medical Journal* 1972; **4:** 7–12.
4. Lundgren S. Sedation as an alternative to general anaesthesia. *Acta Anaesthesiologica Scandinavica* 1987; **32** (Suppl. 88): 21–3.
5. Hempenstall PD, Campbell JPS, Bajurnow AT, Reade PC, McGrath B, Harrison LC. Cardiovascular, biochemical, and hormonal responses to intravenous sedation with local analgesia versus general anesthesia in patients undergoing oral surgery. *Journal of Oral and Maxillofacial Surgery* 1986; **44:** 441–6.
6. Bennett CR. Conscious sedation: An alternative to general anaesthesia. *Journal of Dental Research* 1984; **63:** 832–33.
7. National Institutes of Health: Consensus development conference statement on anaesthesia and sedation in the dental office. *Journal of American Dental Association* 1985; **111:** 90–3.
8. Adam HK, Briggs LP, Bahar M, Douglas EJ, Dundee JW. Pharmacokinetic evaluation of ICI 35868 in man. Single induction doses with different rates of injection. *British Journal of Anaesthesia* 1983; **55:** 97–102.
9. Logan MR, Duggan JE, Levack ID, Spence AA. Single-shot i.v. anaesthesia for outpatient dental surgery. Comparison of 2,6 di-isopropyl phenol and methohexitone. *British Journal of Anaesthesia* 1987; **59:** 179–83.
10. Doze VA, Westphal LM, White PF. Comparison of propofol with methohexital for outpatient anesthesia. *Anesthesia and Analgesia* 1986; **65:** 1189–95.
11. MacKenzie N, Grant IS. Propofol for intravenous sedation. *Anaesthesia* 1987; **42:** 3–6.
12. Newman LH, McDonald JC, Wallace PGM, Ledingham IMcA. Propofol infusion for sedation in intensive care. *Anaesthesia* 1987; **42:** 929–37.
13. Beller JP, Pottecher T, Lugnier A, Mangin P, Otteni JC. Prolonged sedation with propofol in ICU patients: Recovery and blood concentration changes during periodic interruptions in infusion. *British Journal of Anaesthesia* 1988; **61:** 583–8.
14. Smith JM, Misiak H. Critical flicker frequency (CFF) and psychotropic drugs in normal human subjects—a review. *Psychopharmacologia* 1976; **47:** 175–82.
15. Hannington-Kiff JG. Measurement of recovery from outpatient general anaesthesia with simple ocular test. *British Medical Journal* 1970; **3:** 132–5.
16. Maxwell C. Sensitivity and accuracy of the visual analoque scales: a psycho-physical classroom experiment. *British Journal of Clinical Pharmacology* 1978; **6:** 15–24.
17. Scheinin M, Koulu M, Laurikainen E, Allonen H. Hypokalaemia and other non-bronchial effects of inhaled fenoterol and salbutamol: a placebo-controlled dose-response study in healthy volunteers. *British Journal of Clinical Pharmacology* 1987; **24:** 645–53.
18. Fyhrquist F, Wallenius M, Hollemans HJG. Radioimmunoassay of vasopressin in unextracted plasma. *Scandinavian Journal of Clinical and Laboratory Investigation* 1976; **36:** 841–7.
19. Viinamäki O, Erkkola R, Kanto J. Plasma vasopressin concentrations and serum vasopressinase activity in pregnant and nonpregnant women. *Biological Research in Pregnancy and Perinatology* 1986; **1:** 17–9.
20. Winer BJ. *Statistical principles in experimental design*, 2nd edn. New York: McGraw Hill, 1971: 523–46.
21. Harder F, Elsass P, Hendel J, Hvidberg EF, Hjorting-Hansen E. Clinical and psychological effects of intravenous diazepam related to plasma levels. A controlled, double blind, cross over study in oral surgery involving local analgesia. *International Journal of Oral Surgery* 1976; **5:** 226–39.
22. Dionne RA. Differential pharmacology of drugs used for intravenous pre-medication. *Journal of Dental Research* 1984; **63:** 842–7.
23. Lundgren S, Rosenquist JB. Comparison of sedation, amnesia, and patient comfort produced by intravenous and rectal diazepam. *Journal of Oral and Maxillofacial Surgery* 1984; **42:** 646–50.
24. Skelly AM, Boscoe MJ, Dawling S, Adams AP. A comparison of diazepam and midazolam as sedatives for minor oral surgery. *European Journal of Anaesthesiology* 1984; **1:** 253–67.
25. Korttilla K, Tarkkanen J. Comparison of diazepam and midazolam for sedation during local anaesthesia for bronchoscopy. *British Journal of Anaesthesia* 1985; **57:** 581–6.
26. Dixon, J, Power SJ, Grundy EM, Lumley J, Morgan M. Sedation for local anaesthesia. Comparison of intravenous midazolam and diazepam. *Anaesthesia* 1984; **39:** 372–6.
27. Manner T, Kanto J, Salonen M. Use of simple tests to determine the residual effects of the analgesic component of balanced anaesthesia. *British Journal of Anaesthesia* 1987; **59:** 978–82.
28. Valtonen M, Kanto J, Klossner J. Anaesthesia for cardioversion: a comparison of propofol and thiopentone. *Canadian Journal of Anaesthesia* 1988; **35:** 479–83.
29. Valtonen M, Kanto J, Rosenberg P. Comparison of propofol and thiopentone for induction of anaesthesia in elective Caesarean section. *Anaesthesia* 1989; **44:** 758–62.
30. Brandenberger G, Follenius M. Variations diurnes de la cortisolémie, de la glycémie et du cortisol libre urinaire chez l'homme au repos. *Journal de Physiologie* 1973; **66:** 271–82.
31. Hossmann V, Maling TJB, Hamilton CA, Reid JL, Dollery CT. Sedative and cardiovascular effects of clonidine and nitrazepam. *Clinical Pharmacology and Therapeutics* 1980; **28:** 167–76.
32. Grossman A, Besser GM, Milles JJ, Baylis PH. Inhibition of vasopressin release in man by an opiate peptide. *Lancet* 1980; **2:** 1108–10.

Anaesthesia, 1989, Volume 44, pages 735–738

Outpatient paediatric dental anaesthesia

A comparison of halothane, enflurane and isoflurane

M. SIMMONS, C. D. MILLER, G. C. CUMMINGS AND J. G. TODD

Summary

One hundred and fifty unpremedicated children who presented for dental extractions were anaesthetised with nitrous oxide and halothane, enflurane or isoflurane. Ventricular arrhythmias occurred only in the halothane group (14%). Respiratory problems and desaturation were significantly more common in the isoflurane group. Induction times differed significantly between the groups halothane < enflurane < isoflurane, while recovery time and induction to recovery time were significantly shorter in the enflurane group. We suggest that enflurane is the most suitable agent for anaesthetising these patients.

Key words

Anaesthesia; outpatient, paediatric, dental.
Anaesthetics, volatile; halothane, enflurane, isoflurane.

Dental anaesthesia for unpremedicated paediatric outpatients is traditionally by inhalation. In the United Kingdom halothane is still the most widely used volatile agent for this purpose because of its comparative ease of administration.[1] Its use is associated with a significant incidence of arrhythmias[2,3] and the rare complication of hepatotoxicity. Enflurane and isoflurane are less arrhythmogenic[4] and theoretically have the potential for more rapid induction and recovery than halothane. These advantages may be offset by the more irritant effect of isoflurane on the airway and the lesser potency of enflurane. The aim of this study was to assess these three agents for cardiovascular and respiratory side effects in paediatric outpatient dental anaesthesia.

Methods

One hundred and fifty unpremedicated children (3–10 years old, ASA grade 1) who presented for dental extraction under general anaesthesia were randomly allocated into three groups of 50. Each group received halothane, enflurane or isoflurane in 70% nitrous oxide and oxygen for induction and maintenance of anaesthesia. Children who had received a general anaesthetic within the last 6 months, those who were very distressed or those who required elective intubation were not studied. The study was approved by the Ethics Committee.

Anaesthesia was induced in the reclining position with a total fresh gas flow of 9 litres/minute delivered from a machine fitted with a Quantiflex gas mixer and administered through a scavenged coaxial (Bain) breathing system and nasal mask. The chosen volatile agent was delivered from a concealed 'Tec' vaporizer and increased as clinically tolerated to a maximum of 5% for each agent. All inductions were performed by experienced consultant dental anaesthetists (J.G.T. or G.C.C.), and the observers (C.M. or M.S.) were unaware of the volatile agent used. Baseline readings of heart rate (HR), systolic arterial pressure (SAP) and oxygen saturation ($Sa\text{o}_2$) were noted, and thereafter at one-minute intervals from the start of induction. The end of induction was taken as the time when the gag was inserted and was judged by the anaesthetist according to eye position, pattern of breathing and degree of jaw relaxation. The incidence of coughing, laryngospasm, breath-holding and arrhythmias were noted during anaesthesia. The anaesthetist was free to increase the inspired oxygen concentration ($F\text{io}_2$), change the volatile agent, insert a nasopharyngeal airway or tracheal tube when side effects occurred.

All operations were performed by one of two experienced dentists. The number of teeth extracted was recorded. End of anaesthesia was taken as the time when the gag was finally removed, and recovery time from this point to when the child stuck out his tongue to command. The blinding technique was tested when the observer was asked to guess which volatile agent was used.

The data are presented as mean (SD). Statistical analyses of the results were performed using the Chi-squared test,

---

M. Simmons, MB, ChB, FFARCS, Registrar, C.D. Miller, MB, ChB, FFARCS, Senior Registrar, G.C. Cummings, MB, ChB, FFARCS, J.G. Todd, MB, ChB, FFARCS, Consultants, Division of Anaesthesia, Western Infirmary, Dumbarton Road, Glasgow G11 6NT.

Accepted 2 March 1989.

0003–2409/89/090735+04 $03.00/0

© 1989 The Association of Anaesthetists of Gt Britain and Ireland

Table 1. Demography.

Group	Sex M/F	Age, years, mean (SD)	Teeth extracted, mean (SD)
Halothane ($n=50$)	23/27	5.56 (2.11)	1.99 (1.09)
Enflurane ($n=50$)	24/26	5.27 (1.68)	1.82 (1.05)
Isoflurane ($n=50$)	32/18	5.60 (2.10)	1.95 (1.26)
Test	Chi-squared	ANOVA	ANOVA
Significance	ns	ns	ns

Kruskal–Wallis test, Fisher's exact test, and analysis of variance (ANOVA). A p value < 0.05 was considered statistically significant.

Results

There were no significant differences between the three groups with respect to age, male to female ratio, or number of teeth extracted. These results are shown in Table 1.

Induction and recovery times. The time taken from the start of induction to insertion of the gag is a measure of the speed of induction. There was a significant difference in this measurement between the groups (isoflurane > enflurane > halothane). The time taken from insertion of the gag to its removal is a measure of the duration of surgery. This did not differ between the groups. The time taken from removal of the gag to the child sticking out his (her) tongue is a measure of the rate of recovery and was significantly less in the enflurane group. The time from the start of induction to the child sticking out his (her) tongue was significantly less in the enflurane group (Table 2).

Respiratory variables. The isoflurane group showed a significantly increased incidence of coughing, breath-holding, laryngospasm, and laryngospasm that required treatment. The inspired isoflurane concentration was reduced in three of the 12 children; in one of these children the FiO_2 was increased. The FiO_2 was increased in the remaining nine children. Three children were changed to halothane, one of whom required tracheal intubation. The isoflurane group also had a significantly lower mean minimum oxygen saturation. These results are shown in Table 3. The number of children with an oxygen saturation less than 85% was (halothane 3, enflurane 5 and isoflurane 18) significantly greater in the isoflurane group compared with those given halothane ($p < 0.001$) or enflurane ($p < 0.005$).

Cardiovascular variables. The incidence of arrhythmias is given in Table 4. The frequency of atrial arrhythmias at around 8% did not differ for the three agents. Ventricular arrhythmias occurred only with halothane and were present in 14% of cases ($p = 0.001$). In two of the seven children, the only treatment was a reduction in the inspired halothane concentration, in three the arrhythmia settled spontaneously and in the remaining two children the arrhythmias were considered serious enough to require a substitution of enflurane for halothane. The data for systolic arterial pressure and heart rate are given as maximum percentage increases and decreases compared with the pre-induction values (Table 5). There was no difference in the maximum percentage increase in systolic arterial pressure between the groups. The maximum percentage increase in heart rate was greatest with isoflurane. The maximum percentage decrease in systolic pressure and heart rate was less in the isoflurane group. Patients in the latter group with an arterial oxygen saturation less than 85% had a significantly greater increase in blood pressure compared with those whose saturation was greater than 85% ($p < 0.025$).

Induction and operating conditions. The blinded observer judged the number of smooth inductions to be fewer in those who received isoflurane (halothane 46, enflurane 43, isoflurane 23). This was significant $p < 0.001$. There was no difference in the quality of the operating conditions as judged by the dentist (halothane 48, enflurane 44, isoflurane 43 judged as good). The blinded observer correctly guessed the volatile agent on 31, 19 and 27 occasions for the halothane, enflurane and isoflurane groups respectively. These differences were not significant.

Discussion

Enflurane in this study performed as well as or better than either halothane or isoflurane for the induction and maintenance of anaesthesia in unpremedicated children who presented for outpatient dental extractions. The study examined the agents in two ways, namely ease of use and side effects.

Ease of use. Compared with halothane or enflurane, isoflurane was significantly less efficient at producing smooth induction of anaesthesia due to its higher incidence of respiratory side effects. Isoflurane also had the longest induction times. These effects are due to its pungent

Table 2. Induction, operation and recovery times. H, halothane; E, enflurane; I, isoflurane.

Group	Induction to gag in, minutes, mean (SD)	Gag in to gag out, minutes, mean (SD)	Gag out to tongue out, minutes, mean (SD)	Total time, minutes, mean (SD)
Halothane ($n=50$)	2.41 (0.66)	1.66 (2.40)	6.41 (3.28)	10.48 (4.54)
Enflurane ($n=50$)	2.75 (0.75)	1.40 (1.21)	4.11 (1.68)	8.28 (2.54)
Isoflurane ($n=50$)	3.46 (1.71)	1.46 (1.20)	5.71 (2.31)	10.53 (3.20)
Test	Kruskal–Wallis	ANOVA	ANOVA	ANOVA
Significance	H<E $p<0.025$ E<I $p<0.001$	ns	E<H=I $p<0.005$	E<H $p<0.005$ E<I $p<0.005$

Table 3. Respiratory variables. H, halothane; E, enflurane; I, Isoflurane.

Group	Cough	Breath-holding	Laryngospasm	Laryngospasm that required treatment	Minimum Sao_2, mean (SD)
Halothane ($n=50$)	6	5	3	2	94 (11)
Enflurane ($n=50$)	6	6	4	3	92 (13)
Isoflurane ($n=50$)	18	21	21	12	85 (15)
Test	Chi-squared $I>H=E$	Chi-squared $I>H=E$	Chi-squared $I>H=E$	Chi-squared $I>H=E$	ANOVA $I<H=E$
Significance	$p<0.01$	$p<0.001$	$p<0.001$	$I>E$ $p<0.05$ $I>H$ $p<0.01$	$p<0.005$

ethereal odour and irritant effect on the respiratory tract. Both the anaesthetists involved were experienced in the administration of isoflurane and used clinical signs to gauge the rate at which anaesthesia was induced. There was no learning curve effect on the incidence of respiratory problems. The increased incidence of respiratory side effects with isoflurane agrees with the findings of Pandit and co-workers[5] and also with the subgroup of unpremedicated children in Wren's study.[6] Halothane and enflurane produced equally good induction conditions and low rates of respiratory side effects.

The more rapid induction and longer recovery times found in the halothane group are due to its higher potency and solubility. Our findings differed from a recent study of outpatient anaesthesia by Milligan and colleagues[7] who showed that the initial clinical recovery was significantly faster after halothane than after isoflurane. There was no difference in the quality of operating conditions between the three agents despite the differences in MAC. The longer recovery times after isoflurane compared with enflurane are probably due to the longer induction times. The induction to recovery times were shortest with enflurane; this reflects the relative ease of its use.

Side effects. Respiratory side effects were more frequent and severe in the isoflurane group. This is reflected by the lower average minimum arterial oxygen saturation and greater number of patients with a minimum saturation less than 85%. These findings are in agreement with those of Phillips and his co-workers.[8]

High circulating catecholamine levels are associated with cardiac arrhythmias, and in these circumstances halothane is more arrhythmogenic than either enflurane or isoflurane. Our results bear this out and agree with the findings of Casson and Jones.[4] Dental extractions under local anaesthesia are associated with fewer arrhythmias[9] and Kaufman[10] found that the peri-odontal injection of lignocaine helped to prevent cardiac irregularities. Arrhythmias occur when the fifth cranial nerve is stimulated during trigeminal root section.[11] This afferent stimulation effect may be additive to any arrhythmogenic effect of halothane.

All the ventricular arrhythmias occurred in the halothane group and in the absence of significant arterial oxygen desaturation. In contrast, ventricular arrhythmias did not occur with isoflurane despite the significantly greater incidence of arterial desaturation. Four of the six episodes of nodal rhythm in the isoflurane group occurred in children with laryngospasm (mean minimum oxygen saturation 67%), one of whom was given halothane as part of the treatment.

Isoflurane is a more potent peripheral vasodilator than halothane or enflurane and should be associated with a lower arterial blood pressure and a higher heart rate. Hypoxia-induced catecholamine release will modify these effects and may explain the significantly higher heart rates and systemic arterial pressures in the isoflurane group.

The low incidence of side effects with enflurane, coupled with the relative specificity of side effects for the other agents accounts for the greater frequency with which the blinded observer correctly guessed the agent used in the halothane and isoflurane groups.

Table 4. Incidence of arrhythmias.

Group	Atrial arrhythmia	Ventricular arrhythmia	Ventricular arrhythmia that required treatment
Halothane ($n=50$)	4	7	4
Enflurane ($n=50$)	3	0	0
Isoflurane ($n=50$)	6	0	0
Test	Chi-squared	Fisher's exact	Fisher's exact
Significance	ns	$p<0.001$	$p<0.01$

Table 5. Changes in systemic arterial pressure (SAP) and heart rate (HR).

Group	SAP maximum % increase mean (SD)	SAP maximum % decrease mean (SD)	HR maximum % increase mean (SD)	HR maximum % decrease mean (SD)
Halothane ($n=50$)	11.5 (28.0)	16.7 (17.2)	22.1 (24.7)	8.9 (15.8)
Enflurane ($n=50$)	10.8 (21.2)	14.7 (13.2)	24.7 (24.4)	8.3 (17.6)
Isoflurane ($n=50$)	18.8 (20.3)	4.0 (14.5)	47.8 (33.3)	−2.3 (25.9)
Test (ANOVA)	ns	$H=E>I$ $p<0.005$	$I>H=E$ $p<0.005$	$H=E>I$ $p<0.025$

In conclusion, halothane was associated with a high incidence of ventricular arhythmias, while isoflurane had a high incidence of respiratory problems and decreased Sa_{O_2}. Enflurane had a low incidence of side effects, provided satisfactory operating conditions and a shorter procedure time.

Acknowledgments

We thank Dr F.E. Bennetts (Medical Adviser, Abbott Laboratories) for helpful discussions, and Abbott Laboratories for financial support. We also thank Dr G. Murray (University Department of Surgery, Western Infirmary) for guidance on the statistical analysis.

References

1. BRAID DP. Anaesthesia for dental surgery. In: NIMMO WS, SMITH G, eds. *Anaesthesia, Vol. 1.* Oxford: Blackwell Scientific, 1989: 654–64.
2. PLOWMANN PE, THOMAS WJW, THURLOW AC. Cardiac dysrhythmias during anaesthesia for oral surgery. The effect of local blockade. *Anaesthesia* 1974; **29:** 571–5.
3. WHALLEY DG, TIDNAM PF, TYRRELL MF, THOMPSON DS. A comparison of the incidence of cardiac arrhythmias during two methods of anaesthesia for dental extractions. *British Journal of Anaesthesia* 1976; **48:** 1207–10.
4. CASSON WR, JONES RM. Cardiac rate and rhythm during anaesthesia for dental extraction. A comparison of halothane, enflurane and isoflurane. *British Journal of Anaesthesia* 1985; **57:** 476–81.
5. PANDIT UA, STEUDE GM, LEACH AB. Induction and recovery characteristics of isoflurane and halothane anaesthesia for short outpatient operations in children. *Anaesthesia* 1985; **40:** 1226–30.
6. WREN WS, MCSHANE AJ, MCCARTHY JG, LAMONT BJ, CASEY WF, HANNON VM. Isoflurane in paediatric anaesthesia. Induction and recovery from anaesthesia. *Anaesthesia* 1985; **40:** 315–23.
7. MILLIGAN KR, HOWE JP, DUNDEE JW. Halothane and isoflurane in outpatient anaesthesia. A comparison of recovery. *Anaesthesia* 1988; **43:** 2–4.
8. PHILLIPS AJ, BRIMACOMBE JR, SIMPSON DL. Anaesthetic induction with isoflurane or halothane. Oxygen saturation during induction with isoflurane or halothane in unpremedicated children. *Anaesthesia* 1988; **43:** 927–9.
9. RYDER W. The electrocardiogram in dental anaesthesia. *Anaesthesia* 1970; **25:** 46–62.
10. KAUFMAN L. Cardiac arrhythmias in dentistry. *Lancet* 1965; **2:** 287.
11. HUNTER AR. *Neurosurgical anaesthesia.* Oxford: Blackwell Scientific, 1964.

Anaesthesia, 1989, Volume 44, pages 739–741

Effect of intravenous cimetidine on lignocaine disposition during extradural Caesarean section

R. J. FLYNN, J. MOORE, P. S. COLLIER AND P. J. HOWARD

Summary

We studied whether an intravenous bolus of cimetidine altered the disposition of extradurally administered lignocaine in the parturient. Mothers who requested extradural analgesia for elective Caesarean section were randomly pretreated with either cimetidine 200 mg intravenously ($n = 5$) or no H_2-receptor antagonist ($n = 5$). No difference was found between peak plasma lignocaine levels or area under the plasma concentration/time curve between the two groups after administration of 6 mg/kg lignocaine 2% with adrenaline 1:200 000. There was no evidence for an effect of a single intravenous dose of cimetidine on lignocaine disposition in the obstetric patient. In addition, the extradural administration of 6 mg/kg lignocaine produces plasma levels well below toxic levels.

Key words

Anaesthetic techniques, regional; extradural.
Anaesthesia; obstetric.

The administration of H_2-receptor antagonists to decrease gastric acidity before extradural anaesthesia for elective Caesarean section is recommended.[1] However, reports that cimetidine decreases the hepatic clearance of lignocaine has favoured the use of ranitidine. Studies in volunteers have shown that cimetidine decreases lignocaine clearance by inhibition of liver enzyme activity and reduction of liver blood flow.[2] Cimetidine binds to the hepatic cytochrome enzyme system P450 to produce competitive inhibition of the oxidative reactions N-dealkylation and aromatic hydroxylation,[3] which occur in the biotransformation pathways of amide local anaesthetics. Therefore pretreatment with H_2-receptor antagonists might result in toxic plasma levels of lignocaine and bupivacaine. It has been suggested that since large doses of these two local anaesthetics are used for obstetric extradural anaesthesia, that plasma levels of both should be studied in patients given prior cimetidine treatment.[4] Two recently published reports have shown that cimetidine has no affect on bupivacaine concentrations in the obstetric patient.[5,6] Lignocaine is now preferred by many anaesthetists because it has a more rapid onset of action than bupivacaine. This study was undertaken to detail the affect of cimetidine on plasma lignocaine levels during extradural analgesia for elective Caesarean section.

Methods

Only healthy women (36 weeks' or more gestation) who selected extradural anaesthesia for elective Caesarean section were included. They were not receiving any medication apart from maintenance iron therapy. Patient and Medical Research Ethics Committee approval was obtained.

Mothers were randomly allocated to receive either cimetidine 200 mg intravenously, immediately before institution of the extradural block, or no H_2-receptor antagonist. One litre of compound sodium lactate solution was infused during the establishment of extradural anaesthesia. Left lateral tilt (15°) was maintained throughout. An extradural catheter was inserted through the L_{3-4} interspace using a 16-gauge Tuohy needle, with approximately 3–4 cm inside the extradural space. Each mother received 6 mg/kg of preservative-free lignocaine 2% with freshly added adrenaline 1:200 000 (5 μg/ml). A 2-ml test dose was injected through the extradural catheter, followed by a further 8 ml, with the remaining aliquot given as the second dose 5 minutes later. This gave satisfactory analgesia to the level of the sixth thoracic dermatome in all cases. The results from any mother who required additional doses during surgery were eliminated from the study.

R.J. Flynn, FFARCS, Senior Tutor, J. Moore, MD, PhD, FFARCS, Senior Lecturer, P.J. Howard, FIMLS, Technician, Department of Anaesthetics, P.S. Collier, PhD, Senior Lecturer in Pharmacy, Department of Pharmacy, The Queen's University of Belfast, Whitla Medical Building, 97 Lisburn Road, Belfast, Northern Ireland BT9 7BL.
Correspondence to Dr J. Moore please.
Accepted 22 February 1989.

0003–2409/89/090739+03 $03.00/0 © 1989 The Association of Anaesthetists of Gt Britain and Ireland

Arterial pressure was measured at 2-minute intervals until delivery and thereafter every 5 minutes using an Accutor 1A automatic recorder. Hypotension, judged as a decrease in systolic blood pressure below 100 mmHg was treated by increasing the infusion rate and, if necessary, 10 mg ephedrine intravenously.

Venous blood samples were taken from an indwelling catheter in the noninfused arm before any local anaesthetic was given (control sample) and then 5, 10, 15, 20, 25, 30, 40, 50, 60, 70, 80, 90, 120, 180, 240 and 300 minutes after the initial 200-mg dose of lignocaine. Umbilical venous samples were taken from the cord at delivery of the infant. Each sample was centrifuged and the supernatant plasma stored at −20°C until analysis. Lignocaine analysis was by HPLC using mepivacaine as the internal standard. The coefficient of variation of the method of estimation was 9% at 800 ng and 6% at 3000 ng.

All results are presented as mean values (SD); plasma lignocaine levels are shown with 95% confidence intervals. Significance of the differences was calculated using the unpaired *t*-test for demographic data and one-way analysis of variance (ANOVA) for plasma lignocaine levels.

Results

Ten patients were included; five received cimetidine and five had no H_2-receptor antagonist. Both groups were similar for age and weight. Each patient received 6 mg/kg lignocaine and the mean total dose was similar for both groups, namely 456 (73) mg and 432 (74) mg for cimetidine and control respectively. Hypotensive episodes occurred in two patients from each series, and single ephedrine treatment was required in one patient from each group.

The mean plasma concentrations obtained at the various sampling times are shown in Figure 1 and at no time were the differences between the two series statistically significant. The maximum concentration (C_{max}) for both groups and the time of its occurrence (T_{max}) are shown in Table 1. The area under the plasma concentration/time curve (AUC), calculated using the trapezoidal rule, is also shown in Table 1. None of the differences was statistically significant.

The mean elimination half-lives of lignocaine (Table 1) were calculated by linear regression using the natural logarithm of the terminal concentration data. Again none of the differences shown was statistically significant. The difference in standard deviation between the two groups was due to a single outlier in the cimetidine group.

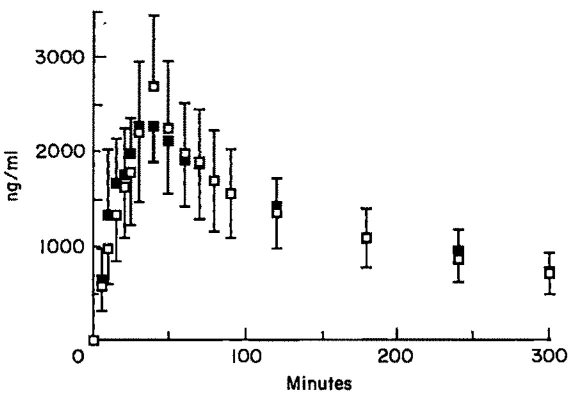


Fig. 1. Mean plasma lignocaine levels (95% confidence intervals). ■, cimetidine; □, control.

Table 1. Pharmacokinetic data, mean values (SD).

	Cimetidine	Control
AUC (ng/ml/minute)	392 181 (58 983)	384 010 (93 154)
$T_{\frac{1}{2}}\beta$ (minute)	246 (164)	196 (25)
C_{max} (ng/ml)	2394 (402)	2693 (758)
T_{max} (minute)	32 (8)	40 (0)

Apgar scores varied between 7 and 9 at one minute and between 8 and 10 at 5 minutes and were similar in both groups. The umbilical venous lignocaine levels and umbilical vein/maternal vein ratios were similar for both groups (Table 2). Maternal vein concentrations refer to the sample nearest the time of delivery.

Discussion

Cimetidine provides effective reduction of acidity and volume of gastric contents for elective obstetric surgery.[7] Here the H_2 blocker was given intravenously to avoid the variable absorption factors associated with oral and intramuscular administration, and the dose produced effective therapeutic plasma levels.[8] Intravenous cimetidine does not effect uterine contractility, fetal heart rate or newborn wellbeing.[9] Lignocaine has a high hepatic extraction ratio (0.7) and its clearance is sensitive to reduction in liver blood flow.[3] The effect of cimetidine on hepatic blood flow is controversial. Feely *et al.*[10] reported a decrease as measured by clearance of the nonmetabolised dye indocyanine green. These workers gave six volunteers a single 600-mg oral dose of cimetidine, followed one hour later by an intravenous bolus of indocyanine green, and a 25% reduction in liver blood flow was found. These findings have subsequently been questioned because clearance is a function of both liver blood flow and hepatic extraction, and changes in indocyanine green extraction could explain these results.[11] Samanta *et al.*[12] failed to show any decrease in hepatic blood flow with cimetidine. The findings reported here agree with this conclusion, since the other main cause of decreased liver blood flow, namely hypotension associated with the extradural block, was equally distributed between the treated and untreated groups.

Cimetidine is an imidazole derivative, a known inhibitor of cytochrome P450, probably because of its ability to inhibit the binding sites for both substrate and oxygen.[13] Lignocaine is metabolised in the liver by the microsomal mixed function oxidase systems, by dealkylation to monoethylglycine and xylidide. The latter has significant local anaesthetic action and 75% of xylidide is excreted in the urine as the further metabolite 4 hydroxy 2,6 dimethylaniline.[3] The rate of drug biotransformation by the mixed

Table 2. Infant blood results, mean values (SD).

	Cimetidine	Control
Maternal vein levels (ng/ml)	2262 (428)	2418 (705)
Umbilical vein levels (ng/ml)	930 (180)	922 (162)
UV/MV ratio	0.42 (0.13)	0.39 (0.06)

function oxidases is determined by the concentration of cytochrome P450, the proportions of the various forms of cytochrome P450 and their affinities for the substrate, and the concentration of cytochrome reductase and the rate of reduction of the drug-cytochrome P450 complex. This study did not demonstrate any inhibition of metabolism, as shown by the insignificant variation in the AUC and elimination half-life values between the two groups. It may be that a single dose of cimetidine is insufficient to produce marked inhibition of the enzyme P450. The large individual variations in the plasma lignocaine levels may also have contributed, and perhaps estimation of the plasma levels of xylidine, a metabolite of this local anaesthetic, would have been a more sensitive test.

In a preliminary report, Dailey *et al.*[14] noted that plasma lignocaine levels were higher after pre-anaesthetic intramuscular cimetidine than after oral ranitidine in patients given 25 ml 2% lignocaine with 1:200 000 adrenaline extradurally for elective Caesarean section. The significant variations in plasma levels occurred at 12, 15, and 18 minutes after lignocaine administration. These workers did not report other pharmacokinetic comparisons, namely AUC or elimination half-life, and the significant differences occurred during the main absorption phase of the local anaesthetic from the extradural space. Their period of sampling was shorter than that of this study and it is impossible to draw further conclusions from their findings.

The plasma lignocaine levels found in all patients included in this study are well below the toxic range,[15] which indicated that this method of lignocaine administration is a safe and effective method of providing extradural analgesia in the obstetric patient. The highest recorded plasma concentration in the series as a whole was 3269 ng/ml, which occurred at 40 minutes in a patient who did not receive cimetidine. This investigation has produced no evidence that pretreatment with intravenous cimetidine effects plasma lignocaine levels.

References

1. MOIR DD. Local anaesthetic techniques in obstetrics. *British Journal of Anaesthesia* 1986; **58:** 747–59.
2. FEELY J, WILKINSON GR, MCALLISTER CB, WOOD AJJ. Increased toxicity and reduced clearance of lidocaine by cimetidine. *Annals of Internal Medicine* 1982; **96:** 592–4.
3. RITCHIE JM, GREENE NM. Local anesthetics. In: GOODMAN LS, GILMAN AG. *The pharmacological basis of therapeutics* 7th edn. New York: Macmillan, 1985: 310.
4. HODGKINSON R. Potential interactions between cimetidine and amide local anesthetics in obstetrics. *Anesthesiology* 1984; **60:** 508.
5. FLYNN RJ, MOORE J, COLLIER PS, MCCLEAN E. Does pretreatment with cimetidine and ranitidine affect the disposition of bupivacaine? *British Journal of Anaesthesia* 1989; **62:** 87–91.
6. O'SULLIVAN GM, SMITH M, MORGAN B, BRIGHOUSE D, REYNOLDS F. H_2 antagonists and bupivacaine clearance. *Anaesthesia* 1988; **43:** 93–5.
7. MCCAUGHEY W, HOWE JP, MOORE J, DUNDEE JW. Cimetidine in elective Caesarean section. *Anaesthesia* 1981; **36:** 167–72.
8. MANCHIKANTI L, KRAUS JW, EDDS SP. Cimetidine and related drugs in anesthesia. *Anesthesia and Analgesia* 1982; **61:** 595–608.
9. MCGOWAN WAW. Safety of cimetidine in obstetric patients. *Proceedings of the Royal Society of Medicine* 1979; **72:** 902–7.
10. FEELY J, WILKINSON GR, WOOD AJJ. Reduction of liver blood flow and propranalol metabolism by cimetidine. *New England Journal of Medicine* 1981; **304:** 692–5.
11. SOMOGYI A, MUIRHEAD M. Pharmacokinetic interactions of cimetidine. *Clinical Pharmacokinetics* 1987; **12:** 321–66.
12. SAMANTA A, MANZI D, LEEVY CM. Evaluation of cimetidine induced hepatic abnormalities by Fick principle studies. *Gastroenterology* 1983; **84:** 1393.
13. STANSKI DR, WATKINS WD. *Drug disposition in anesthesia. The scientific basis of clinical anesthesia.* New York: Grune and Stratton, 1982: 26.
14. DAILEY PA, HUGHES SC, ROSEN MA, HEALY K, CHEEK DBC, PYTKA S, FISHER DM, SHNIDER SM. Lidocaine levels during cesarean section after pretreatment with ranitidine or cimetidine. *Anesthesiology* 1985; **63:** A444.
15. SHNIDER SM, WAY EL. Plasma levels of lidocaine (Xylocaine) in mother and newborn following obstetrical conduction anesthesia: clinical applications. *Anesthesiology* 1968; **29:** 951–8.

Anaesthesia, 1989, Volume 44, pages 742–746

Advantages of the paramedian approach for lumbar epidural analgesia with catheter technique

A clinical comparison between midline and paramedian approaches

R. G. BLOMBERG, A. JAANIVALD AND S. WALTHER

Summary

Forty-nine patients, scheduled for transurethral resection of the prostate or a bladder neoplasm on 50 occasions, were studied. The patients were randomly allocated to one of the two methods of puncture, midline or paramedian. Technical difficulties and the occurrence of complications were recorded. The extent of sensory and motor blockade was also compared. The paramedian approach was associated with a lower frequency of technical problems compared to the midline approach. Statistically significant differences were demonstrated between the two techniques for the following factors: repeated attempts at needle insertion; difficulty in identification of the epidural space; resistance to introduction of the catheter; resistance to injection through the epidural catheter; and the production of paraesthesiae (nine patients in the midline group compared to only one patient in the paramedian group, $p < 0.01$). The catheter entered a vessel at first in two patients in each group. No significant differences were demonstrated between the groups in the extent of sensory and motor blockade. The study supports the view that the paramedian approach has technical advantages over the midline approach for lumbar epidural analgesia with catheter technique.

Key words

Anatomy; spinal canal, epidural space.
Anaesthetic techniques; epidural.

Advantages of the paramedian approach for lumbar epidural analgesia are claimed by several authors.[1-6] A comparison was made in the same cadaver of the midline and paramedian approaches for lumbar epidural puncture and catheter introduction in a recent study using epiduroscopy in 14 autopsy subjects.[7] Technical advantages of the paramedian approach included a small risk of accidental perforation of the dura mater, no tenting of the dura by the tip of the catheter and the promotion of a straight course cephalad in the near midline for the epidural catheter. The factors responsible for these differences were found to be the different angle of the needle to the dura mater and the restricted mobility of the dura mater caused by the dorsomedian connective tissue band. The combined influence of these two factors was greatest for the midline needle and catheter.

Two clinical studies were presented with a comparison of the two techniques for lumbar epidural analgesia. Jaucot[8] demonstrated in a retrospective study of obstetric analgesia a lower frequency of paraesthesia and of vascular puncture when the paramedian approach was used. Griffin and Scott[9] did not demonstrate any difference in the frequency of technical complications in a prospective study in obstetric analgesia.

The present prospective study was designed to investigate differences between the two techniques for lumbar epidural analgesia with a catheter technique. Attention was paid to ease of identification of the epidural space and to the occurrence of technical problems and complications of needle insertion and catheter introduction. Finally, the extent of sensory and motor blockade was compared in the two groups.

Methods

Forty-nine patients who presented with a diagnosis of hypertrophy of the prostate, neoplasm of the prostate or neoplasm of the bladder were studied. They were scheduled for transurethral resection of the prostate or of bladder malignancy under epidural analgesia on 50 occasions. The patients gave informed consent to participation in the study and were randomly allocated to epidural needle and catheter introduction with either a midline or a paramedian approach. Patients who had a herniation of a lumbar disc

---

R.G. Blomberg, MD, Consultant Anaesthetist, A. Jaanivald, MD, Registrar, S. Walther, MD, Senior Registrar, Department of Anaesthesia, Central Hospital, S-601 82 Norrköping, Sweden in affiliation with the Department of Anaesthesiology, University Hospital, Linköping, Sweden.

Accepted 6 February 1989.

0003–2409/89/090742+05 $03.00/0

© 1989 The Association of Anaesthetists of Gt Britain and Ireland

or any general neurological disorder were excluded from the study.

Assessment before anaesthesia of the patients and all the epidurals were performed by one investigator (R.G.B.) including the evaluation of technical difficulties. The onset and extent of sensory and motor blockade and the quality of analgesia during the operation were determined by one of the other two authors, and included a postoperative examination 2 hours after the operation and an interview the next day. This investigator was unaware of the approach used.

Premedication was administered as an oral mixture of diazepam 12 mg for patients up to 70 years of age and 6 mg if the patient was older. No other sedatives or analgesics were given unless the patient was uncomfortable. Ringer acetate solution 500 ml was infused intravenously before the attempt at epidural. All patients were placed in the left lateral position and the epidural block performed with an 18-G Tuohy needle in the interspace L_{3-4} (except one patient who sat upright because he was unable to lie on his side). Subcutaneous infiltration that included ligaments and periosteum was performed with 5 ml 2% mepivacaine (Carbocaine) with adrenaline 5 μg/ml at room temperature. The midline approach was with a cranial angle of the needle to the dorsal plane of the skin of 90–110°. The paramedian puncture was performed according to Bonica[1] 1.5 cm lateral to the caudal part of the spinous process of L_4. The Tuohy needle, with the orifice pointing cephalad, was then directed towards the midline of the epidural space of L_{3-4}, often after contact of the tip of the needle with the corresponding lamina. The cranial angle of the paramedian needle to the dorsal plane of the skin was 120–135°. The epidural space was identified by loss of resistance to saline in a glass syringe and the position of the needle then immediately locked. Leakage of blood or cerebrospinal fluid (CSF) through the needle was sought. The production of paraesthesiae was noted. An epidural catheter (Vygon, polyamide, 19 G, single orifice) was then introduced 3 cm into the space with the needle orifice still pointing cephalad (except in two subjects, one in each group, in whom it was possible to pass the catheter only 2 cm into the epidural space before resistance was encountered). Resistance to introduction was recorded by the performer of the block, as well as any paraesthesia produced by the catheter. Spontaneous flow of blood or CSF through the catheter was sought and an aspiration test thereafter performed.

The total dose of local anaesthetic (2% mepivacaine with adrenaline 5 μg/ml) was calculated to cover the dermatomes from T_8 to S_5 using the segmental dose requirements in relation to age recommended by Bromage.[10] Injection was only performed through the catheter. A test dose of 5 ml was administered at a rate of 0.5 ml/second. The rest of the total dose was injected at the same rate after a 5-minute period of observation. Any initial resistance to injection through the catheter was recorded.

Blood pressure and heart rates were measured at least every 5 minutes during the onset of the block and throughout the operation. Ephedrine was administered in increments of 5 mg intravenously, in the event of a decrease in systolic blood pressure more than 30 mmHg below the pre-anaesthetic level.

The extent of sensory blockade was determined by the pinprick method at 10, 20 and 30 minutes after the complete injection of local anaesthetic. The degree of motor blockade was established with the aid of a modified Bromage scale.[11] A top-up dose of two-thirds the original total dose of local anaesthetic was administered if there was inadequate analgesia at 30 minutes. A similar top-up dose was given 75 minutes after the previous dose in a prolonged procedure. The patients were observed for at least 2 hours after operation before the epidural catheter was removed and the patient returned to the ward. The catheter was inspected for blood when it was removed.

The patient was interviewed the next day about discomfort or pain during the epidural block procedure, as well as the occurrence of headache or pain in the back.

Statistical analyses. Differences between the two groups in frequency of technical problems were assessed using Fisher's exact test in all cases, except for the number of insertions of the Tuohy needle. An exact randomisation test was applied for this factor. These statistics were performed as single-tailed tests. Incidences of failure of epidural analgesia, hypotension and postoperative back pain were compared using Fisher's exact test and as two-tailed tests. Analyses of differences in extent of sensory and motor blockade were performed with Student's *t*-test and with an exact randomisation test and as two-tailed tests. A p-value < 0.05 was considered significant.

Results

Epidural analgesia was attempted for the urological procedure with the midline approach in 25 subjects and with the paramedian approach in another 25. One patient was studied twice with an interval of 6 months. The randomisation procedure allocated him to the midline group in the first instance and to the paramedian group in the second.

The age range of the midline group was 55–90 years with an average of 72.5 (median 74.0) years, and of the paramedian group 63–84 years with an average of 73.4 (median 73.5) years. The patients were classified as ASA physical status 1 or 2, with the exception of eight (six in the midline group and two in the paramedian) whose status was 3. A summary of the technical problems is presented in Table 1.

The catheter had to be adjusted by withdrawing it 3–5 mm in order to make injection possible, in five of the seven cases with resistance to injection. Blood was initially present in the catheter of two patients in each group. The blood persisted, with the midline technique, in both subjects despite withdrawal of the catheter more than 1 cm, and the epidural method was abandoned. The two paramedian catheters were withdrawn 1 cm, upon which the blood disappeared. An adequate block was achieved in both these patients after a negative test dose. The catheters of three additional subjects, two inserted with a paramedian approach, were found to contain blood on extraction. Initially the block was judged to be adequate, but it subsequently proved to be a partial failure in two of these patients. There was thus evidence of bleeding or intravascular placement in seven patients (14%).

Paraesthesiae were experienced during introduction of the catheter with the midline approach by nine patients, and with the paramedian technique by one patient ($p < 0.01$). No paraesthesiae persisted during injection of local anaesthetic and no neurological sequelae developed.

Resistance to the introduction of the catheter and resistance to injection through the catheter was more common

Table 1. Technical problems of lumbar epidural analgesia in 25 subjects with midline and 25 subjects with paramedian approach.

	Number of subjects		
	Midline $n=25$	Paramedian $n=25$	Probability
Needle problems			
Repeated insertions			
(needle or catheter problems)			
two attempts	5	2	
three attempts	2	0	
Total	7	2	$p<0.05$
Difficult identification of epidural space	6	1	$p<0.05$
Pain on needle insertion	0	0	—
Blood in needle	0	0	—
CSF in needle	0	0	—
Catheter problems			
Resistance to introduction	11	4	$p<0.05$
Paraesthesiae	9	1	$p<0.01$
Resistance to injection	6	1	$p<0.05$
CSF in catheter	0	0	—
Blood in catheter initially	2*	2†	—
Blood in catheter on withdrawal	1	2	ns
No catheter problem	9	19	$p<0.01$
Failure			
complete	2	0	
partial	1	1	
Total	3	1	ns

*Withdrawal of catheters > 1 cm, bleeding persisted. One patient received subarachnoid analgesia and one a general anaesthetic.

†Withdrawal of catheters 1 cm, bleeding stopped. Successful epidural block in both patients.

with the midline technique than with the paramedian approach ($p < 0.05$ in both instances). In four midline cases and the one paramedian, the resistance to injection was so great that it was necessary to withdraw the catheter 3–5 mm in order to make the injection possible. The number of cases with no catheter problem of any sort was nine in the midline group compared to 19 in the paramedian group ($p < 0.01$).

The characteristics of the analgesia and postoperative observations are presented in Table 2. The local anaesthetic dose caused adequate analgesia in all but four patients; two in each group. A top-up dose resulted in the necessary increase of sensory blockade. Six patients in each group had differences in sensory level of the left and right side limited to 1–3 spinal segments, with the exception of one patient in the midline group, where a left-sided-only block developed. Bilateral analgesia was achieved in this patient, adequate for the surgical procedure, after a top-up dose in the supine position. None of the differences between the groups in extent of sensory blockade was statistically significant. Variations between the groups in motor blockade occurred; these were small and without statistical significance. Complete bilateral motor block was present in two patients in each group.

Minor postoperative complaints, without significant differences in relation to approach, were reported by the 49 patients during their postoperative interview. One interview could not be carried out because the patient died. This

Table 2. Comparison of lumbar epidural analgesia in 23 subjects with midline and 25 with paramedian approach, and postoperative observations in 25 patients with midline insertion of needle and 24 with paramedian insertion.

	Number of subjects		
	Midline	Paramedian	Probability
Sensory blockade—number of spinal segments (mean, SD)	17.6 (3.5)	18.1 (2.5)	ns
Ephedrine administration (hypotension)	5	8	ns
Supplementation, midazolam or pethidine, requested by apprehensive patient	2	3	ns
Back pain after operation	5	4	ns
Headache after operation (no relation to patient position)	2	2	—

patient, 77 years of age, with a history of myocardial infarction, was classified as ASA status 3 because of incapacitating myocardiosclerosis and angina pectoris. Epidural analgesia with a paramedian approach without technical problems resulted in an adequate sensory block of T_3–S_5. Initial systolic hypotension from 140 to 95 mmHg was successfully treated with ephedrine 5 mg, after which the patient's condition was stable throughout the operation. He developed signs of a myocardial infarction with cardiogenic shock 4 hours after operation and died despite intensive therapy 4 days later.

Discussion

There are conflicting results in the two systematic studies of comparison between the midline and paramedian approaches. Griffin and Scott,[9] prospectively studied 165 patients with obstetric epidural analgesia and did not establish any significant differences between the two methods. They did not, however, report the occurrence of paraesthesiae during the introduction of the catheter. The retrospective study of Jaucot[8] was performed in 1010 patients with obstetric epidural analgesia; he reported a higher incidence of intravascular placement of the catheter with the midline approach (5.6%) compared to the paramedian (1.5%) and a frequency of initial paraesthesiae of 48% for the midline technique and of 24% for the paramedian.

One of the authors (R.G.B.) has considerable clinical experience with the paramedian approach for lumbar epidural analgesia and prefers it. The present study was performed in male patients in an age group that might be expected to accentuate any technical difficulties. The possibility of an investigator's bias was not completely excluded in this investigation, since the observation of technical problems of epidural puncture and catheter introduction necessarily were made by the performer of the block, despite obvious knowledge of the approach used. The study was, however, carried out as objectively as possible with this source of error in mind.

The production of paraesthesiae during the introduction of an epidural catheter must be taken as an indication of contact, possibly with the spinal cord but more likely, especially in the lumbar region, with a nerve root or a nerve. It may, in the latter event, also be a sign of lateral deviation of the course of the catheter. The results of the present study demonstrate a higher incidence of paraesthesiae for the midline catheter. This agrees with results mentioned earlier from the study with epiduroscopy in autopsy subjects[7] which compared the two techniques and demonstrated a variable course of the midline catheter, often with lateral or caudal deviation. An obvious tendency for the paramedian catheter to pass in a straight course cephalad in the near midline was shown. This accords with the low frequency of paraesthesiae produced by the paramedian catheter.

The production of paraesthesiae in epidural analgesia is not always reported as a complication. Some references in the literature indicate a high frequency; Fortuna[12] states that paraesthesiae are very common. Philip[13] mentions an initial rate of 49% reduced to 29% after the injection of 10 ml of air before introduction of the catheter. Rolbin[14] indicates a frequency of paraesthesiae with two different types of catheter, as 44% and 24% respectively. The approach used was not specified in these three studies, while Jaucot,[8] as stated above, demonstrated a higher frequency for the midline approach. Minor and transient neurological sequelae seldom develop in patients subjected to epidural analgesia, with incidences reported as 0.1%[15] up to 0.4%.[16] Any possible relationship between the production of paraesthesiae and the development of such neurological complications in rare cases still seems to need investigation. However, the low frequency of paraesthesiae demonstrated for the paramedian approach in this study may be a potential advantage in this respect.

This study failed to reveal any differences in intravascular placement between the two techniques. Difficulties in localisation of the epidural space, resistance to catheter introduction and resistance to injection of anaesthetic solution through the catheter were found to be less frequent in the group with the paramedian approach. These observations, with reservations for the possibility of bias, and the low frequency of paraesthesiae with the paramedian technique demonstrate the technical advantages of this approach for lumbar epidural analgesia with a catheter technique.

Acknowledgments

This study, which has been supported by grants from the Fredga Research Foundation, the County Council of Östergötland and by Astra Alab AB, was made possible by the kind cooperation of the staff of the Urology Section, Department of Surgery and the Operations unit, Department of Anaesthesia, Central Hospital, Norrköping.

References

1. Bonica JJ. Continuous peridural block. *Anesthesiology* 1956; **17:** 626–30.
2. Bonica JJ, Backup PH, Anderson CE, Hadfield D, Crepps WF, Monk BF. Peridural block: analysis of 3,637 cases and a review. *Anesthesiology* 1957; **18:** 723–84.
3. Bromage PR. *Epidural analgesia.* Philadelphia: W.B. Saunders, 1978: 187–8.
4. Carrie LES. The approach to the extradural space. *Anaesthesia* 1971; **26:** 252–3.
5. Armitage EN. The paramedian approach to lumbar epidural analgesia. *Anaesthesia* 1976; **31:** 1287–8.
6. Barretto C, Hook R, Seah CH. Use of the Tuohy needle in paramedian approach for peridural block. A study using epiduroscopy in autopsy subjects. *Anesthesia and Analgesia* 1977; **56:** 582–4.
7. Blomberg RG. Technical advantages of the paramedian approach for lumbar epidural puncture and catheter introduction. A study using epiduroscopy in autopsy subjects. *Anaesthesia* 1988; **43:** 837–43.
8. Jaucot J. Paramedian approach of the peridural space in obstetrics. *Acta Anaesthesiologica Belgica* 1986; **37:** 187–92.
9. Griffin RM, Scott RPF. A comparison between the midline and paramedian approaches to the extradural space. *Anaesthesia* 1984; **39:** 584–6.
10. Bromage PR. Ageing and epidural dose requirements. Segmental spread and predictability of epidural analgesia in youth and extreme age. *British Journal of Anaesthesia* 1969; **41:** 1016–22.
11. Bromage PR. A comparison of the hydrochloride and carbon dioxide salts of lidocaine and prilocaine in epidural analgesia. *Acta Anaesthesiologica Scandinavica* 1965; (Suppl. XVI): 55–69.
12. Fortuna A, Brusarosco FF. Clinical evaluation of Citanest in peridural anesthesia. *Acta Anaesthesiologica Scandinavica* 1965; (Suppl. XVI): 223–30.
13. Philip BK. Effect of epidural air injection on catheter complications. *Regional Anesthesia* 1985; **10:** 21–3.

14. Rolbin SH, Hew E, Ogilvie G. A comparison of two types of epidural catheters. *Canadian Journal of Anaesthesia* 1987; **34:** 459–61.
15. Dawkins CJM. An analysis of the complications of extradural and caudal block. *Anaesthesia* 1969; **24:** 554–63.
16. Abouleish E. Neurologic complications following epidural analgesia in obstetrics. One center's experience. *Regional Anesthesia* 1982; **7:** 119–24.

Anaesthesia, 1989, Volume 44, pages 747–749

Regional anaesthesia for surgery of the forearm and hand

A technique of combined supraclavicular and discrete blocks

B. E. SMITH, J. F. CHALLANDS, M. SUCHAK AND D. SIGGINS

Summary

Eighty patients who presented for surgery of the forearm or hand were allocated randomly to one of two groups. In Group A, surgery was performed under supraclavicular brachial plexus block only; a mixture of equal parts of prilocaine 1% and bupivacaine 0.5% without adrenaline was used. In Group B, supraclavicular brachial plexus block was performed using prilocaine 1% alone, but in addition discrete nerve blocks were performed at elbow level using 0.5% bupivacaine without adrenaline. Patients in Group B had a significantly shorter duration of unwanted postoperative motor blockade and a significantly longer duration of postoperative analgesia ($p < 0.005$).

Key words

Pain; postoperative.
Anaesthetic techniques, regional; brachial plexus block, median nerve block, radial nerve block, ulnar nerve block.

Most surgery of the forearm and hand can be performed under regional anaesthesia, particularly brachial plexus block. Ideally, any technique should provide rapid onset of surgical anaesthesia, analgesia of the upper arm to prevent tourniquet pain (if a tourniquet is used), adequate muscular relaxation, a relatively ischaemic field and, if possible, good postoperative analgesia. Prolonged postoperative analgesia may be produced by brachial plexus block with bupivacaine, but the latency may be unacceptably long and unwanted motor block may persist well into the postoperative period. Lignocaine and prilocaine produce a rapid onset of action, but provide analgesia for a relatively short time in the postoperative period.

Many clinicians compromise by using a mixture of local anaesthetic agents for brachial plexus block to produce rapid onset and prolonged duration. There is an alternative approach. Supraclavicular brachial plexus block can be performed with either prilocaine or lignocaine to provide analgesia of the upper arm in order to obtund tourniquet pain, complemented by discrete nerve blocks at the elbow with bupivacaine. Unwanted postoperative motor block of the shoulder and elbow is reduced to a minimum, both in degree and duration, whilst both intra- and postoperative analgesia is improved both in latency and duration.

This study was undertaken to compare these techniques.

Patients and methods

The study was approved by the district ethics committee. Eighty adult patients of ASA grades 1 to 3 who presented for surgery of the forearm or hand were studied. All patients were premedicated with temazepam 20 mg orally 1–2 hours pre-operatively. Each patient was then allocated to one of two groups according to a random number sequence.

Patients in Group A received a supraclavicular brachial plexus block alone using Ball's technique[1] with a peripheral nerve stimulator.[2] The local anaesthetic solution comprised equal volumes of prilocaine 1% and bupivacaine 0.5%, without adrenaline, in a volume of 0.5 ml/kg body weight to a maximum of 40 ml. In Group B, supraclavicular brachial plexus block was performed by the same method but using prilocaine 1% without adrenaline as the sole agent; the volume used was 0.5 ml/kg to a maximum of 40 ml. In addition, discrete nerve blocks of the median, radial, and ulnar nerves as appropriate to the surgical field were performed at elbow level, using 2–5 ml bupivacaine 0.5% without adrenaline. A low-power nerve stimulator was used to aid nerve location in each case. All blocks were performed with a 25-gauge short bevel needle (Retrobulbar needle, 25 g × 40 mm—Steriseal Ltd.).

Analgesia was assessed by loss of sensation to pinprick in the surgical field and the upper arm. Motor blockade was measured at 5-minute intervals by assessment of the power of flexion and extension at the shoulder and elbow, and of grip strength of the hand. The assessments were performed by an observer who was blind to the patient grouping. He used 10-cm visual analogue score lines, where 10 represented full power and zero indicated complete motor block. The final motor score was taken as the greatest change that

---

B.E. Smith, FFARCS, Consultant, J.F. Challands, MB, ChB, Senior House Officer, M. Suchak, FFARCS, D. Siggins, FFARCS, Registrars, Department of Anaesthetics, The Alexandra Hospital, Woodrow Drive, Redditch, Worcs B98 7UB.
Accepted 20 March 1989.

0003–2409/89/090747+03 $03.00/0
© 1989 The Association of Anaesthetists of Gt Britain and Ireland

Table 1. Power of flexion and extension (cm on visual analogue score) at the elbow, and grip strength (cm) immediately before surgery. 10 = normal power, 0 = complete motor block. Values are expressed as mean (range).

	Group A (*n* = 40)	Group B (*n* = 40)	p
Elbow	3.1 (1.1–5.3)	2.6 (0–5.7)	n.s.
Grip	4.4 (2.2–6.4)	2.1 (0–5.3)	<0.025

occurred before surgery started.

In all patients the tourniquet was applied over a layer of orthopaedic wadding and positioned as low as possible on the upper arm. The tourniquet was inflated to 100 mmHg above the systolic arterial pressure after exsanguination of the limb. The total tourniquet time was recorded for each patient.

All patients were monitored throughout the procedure using automated oscillotonometry and a continuous electrocardiogram. The duration of analgesia after operation was assessed by the time to recovery of pinprick sensation or by first complaint of pain, whichever occurred sooner. Motor block of the arm was assessed with the same visual analogue method for both shoulder and elbow power, and grip strength. This assessment was performed by an observer who was blind to the patient grouping.

The data were analysed using the Wilcoxon rank sum test, the Chi-square test or analysis of variance as appropriate.

Results

There were no significant differences between the groups in respect of age, weight, sex, nature of surgery, duration of surgery, tourniquet time or grade of surgeon who performed the operation.

The time from induction of regional anaesthesia to start of surgery was 16 (range 9–26) minutes in Group A and 14 (10–23) minutes in Group B. This difference was not significant.

Pre-operative motor blockade

The results for both groups are shown in Table 1. There was a greater degree of motor block as judged by grip strength in Group B ($p < 0.025$).

Intra-operative analgesia

No patient in either group complained of tourniquet pain. Two patients in Group A reported mild discomfort during initial skin incision, although in neither case was this of sufficient severity to distress the patient or delay surgery.

There were no reports of pain during surgery from any patient in Group B. There were no significant differences between groups in arterial pressure or heart rate during induction or surgery. No adverse effect attributable to the local anaesthetic agents was seen in either group.

Postoperative assessment

The times to return of full motor power in each group are shown in Table 2. Recovery of power in the shoulder and elbow was significantly more rapid in Group B; recovery of grip power was significantly slower in Group B ($p < 0.005$ in each case). The duration of postoperative analgesia was significantly longer in Group B than in Group A (Table 3); this difference was highly significant ($p < 0.005$).

Table 2. Time (hours) from induction of regional block(s) to recovery of full motor power. Values are expressed as mean (range).

	Group A (*n* = 40)	Group B (*n* = 40)	p
Elbow	6.3 (4.8–13.3)	2.3 (1.8–5.5)	<0.005
Grip	5.7 (3.5–12.0)	14.4 (6.5–22.0)	<0.005

Motor block outlasted analgesia in 20 patients. This occurred in 18 patients in Group A and was due to residual motor blockade at the elbow or shoulder in all cases. The interval between the recovery of sensation and motor power was in excess of 4 hours in five patients. Motor blockade outlasted analgesia in two patients in Group B, the longest interval being 1.8 hours; this difference was highly significant ($p < 0.001$). There was no clinical evidence of pneumothorax in any patient. Three patients had a paroxysm of coughing during induction of the supraclavicular brachial plexus block, but postoperative chest radiographs failed to show any pneumothorax.

Discussion

This study has demonstrated that supraclavicular brachial plexus block performed with prilocaine 1% without adrenaline, combined with discrete nerve blocks using bupivacaine, satisfies most of the criteria for an ideal regional anaesthetic technique for surgery of the forearm and hand. The relatively rapid return of motor power to the shoulder and elbow after surgery was a significant advantage of the combined technique, as this resulted in the return of control of the limb. Conversely, the prolonged duration of motor block in excess of analgesia was a prominent feature in Group A. The most striking feature of the combined technique was the duration of postoperative analgesia (mean 12.8 hours); analgesia lasted for more than 16 hours in six patients.

Such prolonged analgesia may have resulted from the time interval between induction of the discrete blocks and application of the tourniquet; in all patients, the brachial plexus block was performed first and the discrete blocks immediately afterwards. The tourniquet was applied usually within 5 minutes of performance of the discrete blocks. There would as a result, be no circulation in the arm below the tourniquet until after surgery was completed; this would prevent significant clearance of bupivacaine from the injection site, thereby increasing the peak intraneural concentration of the anaesthetic during phase I of the block. Evidence suggests that the duration of nerve block is related directly to the peak intraneural concentra-

Table 3. Duration of postoperative analgesia (hours).

	Group A (*n* = 40)	Group B (*n* = 40)	p
Mean	4.7	12.8	<0.005
Range	2.8–10.0	5.5–20.0	

tion of local anaesthetic.[3] This hypothesis is supported by the observation that all six patients who had analgesia for more than 16 hours had a tourniquet time in excess of one hour. The shortest duration of analgesia in Group B was 5.5 hours. This occurred in a patient in whom there was a 30-minute delay between induction of the discrete blocks and tourniquet application. In addition, the tourniquet time in this patient was only 17 minutes.

It was anticipated that the quality of surgical anaesthesia in the combined block group might prove to be superior to the brachial plexus block group. Two patients in Group A reported mild discomfort during initial skin incision compared with no such reports in Group B, but this difference was not significant.

The total volume of local anaesthetic solution employed was greater in Group B than in Group A. However, this does not imply that a greater risk of systemic toxicity existed in Group B. A patient in Group A could receive 20 ml prilocaine 1%, and 20 ml bupivacaine 0.5%, i.e. 200 mg prilocaine and 100 mg bupivacaine. Conversely, a similar patient in Group B received 400 mg prilocaine but only 10–75 mg bupivacaine, depending on the number of discrete blocks performed and the volume employed for each block. Thus, the total dosage of the more toxic bupivacaine was less in Group B. In addition, the systemic absorption of bupivacaine should be delayed because the tourniquet is proximal to the site of nerve block.

The majority of patients underwent extensive hand surgery and significant postoperative pain was likely to persist for a prolonged period. The presence of a 'boxing glove' dressing reduces the importance of delayed return of motor function in the hand. Bupivacaine was considered to be the drug of choice for the discrete blocks in order to provide analgesia for as long as possible. However, the use of a shorter acting agent for the discrete blocks, e.g. prilocaine 2%, might produce a similar qualitative effect of shorter duration. The relative disadvantage of prolonged motor block of the wrist and hand could thus be minimised if this was considered to be desirable.

In this study, supraclavicular brachial plexus block was used because of its rapid onset in comparison to the axillary approach.[4] However, other approaches may produce an equally satisfactory outcome.

Acknowledgments

Our thanks are due to our surgical colleagues, and especially to Mr A. E. Mulira FRCS, and our anaesthetic nurses for their patience and support throughout this study.

References

1. Ball HCJ. Brachial plexus block. A modified supraclavicular approach. *Anaesthesia* 1962; **17:** 269–73.
2. Smith BE. Distribution of evoked paraesthesiae and effectiveness of brachial plexus block. *Anaesthesia* 1986; **41:** 1112–5.
3. Smith BE, Siggins D. Low volume, high concentration block of the sciatic nerve. *Anaesthesia* 1988; **43:** 8–11.
4. Eriksson E. Brachial Plexus Block. In: Eriksson E, ed. *Illustrated handbook of local anaesthesia,* 2nd edn. London: Lloyd-Luke, 1979: 79–84.

Anaesthesia, 1989, Volume 44, pages 750–752

Alteration of maternal posture and its immediate effect on epidural pressure

G. M. JOHNSTON, R. C. RODGERS AND M. E. TUNSTALL

Summary

A study was undertaken to investigate the changes in pressure inside the epidural space in parturients in the first stage of labour. The purpose was to see whether acute local pressure changes in the epidural space were consistent with the hypothesis that there is physical movement of cerebrospinal fluid with certain changes in maternal posture. Pressure changes were measured via the epidural catheter through which continuous infusion epidural analgesia was administered, using a pressure transducer kept at the level of the lumbar spine. The mothers moved through a series of postures that reflected those expected during the course of labour and delivery. The pressure within the catheter was recorded during these manoeuvres. The pressure changes which were found, taken in conjunction with the associated investigations of others, are consistent with the hypothesis.

Key words

Anaesthetic techniques, regional; epidural.
Anaesthesia; obstetric.

The evidence provided in clinical reports[1–3] supports the hypothesis[4] that physical movement of cerebrospinal fluid (CSF) after change of posture is the principal reason for high levels of spinal analgesia in late pregnancy. Acute changes in epidural pressure after alterations in maternal posture could provide indirect evidence in support of the hypothesis.

Epidural pressure is an indirect indicator of CSF pressure,[5] which in turn is a reflection of venous pressure. Change in venous pressure is transmitted directly to the CSF. The 'venous wall' which separates CSF from the thoracic abdominal and external pressures is extremely elastic.[6] There will be a pressure gradient if external pressure on the venous wall suddenly becomes greater in the lumbosacral section than in the thoracic section. It will cause an immediate shift of CSF cephalad, after which CSF pressure will rapidly revert to normal limits. Marx *et al.*,[7] have shown that in the normal pregnant woman at term in the supine position, CSF pressures are within normal limits.

The unique situation in obstetrics is the liability to rapid changes in the degree of inferior vena caval compression with alterations in maternal posture. The changes are reflected in epidural pressure changes. It is necessary to make immediate measurement of epidural pressure after alterations in posture, in order to gain an indication of its likely effect on the movement of CSF.

Sprague[2] found that the most rapidly achieved, as well as the most effective, subarachnoid blocks for Caesarean section were obtained when the mothers received the injection lying on their right sides and were turned immediately through supine to the left semilateral position. Our interpretation is that this would guarantee transient and covert inferior vena caval compression sufficient to cause a cephalad surge of CSF. There is an increase in epidural pressure when posture is altered from lateral to supine even without caval compression.[8] The effect of caval compression is additive. Baseline extradural pressures decrease when it is relieved by left uterine displacement (LUD) in the supine position.[9]

Methods

Fourteen women in labour were studied. Selection criteria demanded that the study group should be fit, healthy parturients with no maternal or fetal pregnancy complications, in established labour. Effective epidural analgesia was necessary, maintained by continuous infusion. Continuous fetal monitoring was a prerequisite for inclusion in the study, as was close monitoring of maternal

---

G.M. Johnston, MB, ChB, FFARCS, R.C. Rodgers, MB, BCh, BAO, FFARCSI, M.E. Tunstall, MB, BS, FFARCS, DObstRCOG, Anaesthetic Department, Aberdeen Royal Infirmary, Aberdeen, Scotland.
Correspondence should be addressed to Dr M.E. Tunstall please.
Accepted 7 March 1989.

0003–2409/89/090750+03 $03.00/0 © 1989 The Association of Anaesthetists of Gt Britain and Ireland

arterial blood pressure during the shifts in posture. All members of the study group gave informed consent, and the study had the approval of the local Medical Ethics Research Committee.

Each epidural anaesthetic was conducted in a prescribed manner. All used identical epidural catheters (Portex nylon, 16-G with three helical eyes), with a three-way tap placed downstream of the Millipore filter and with a calculated length of 5-cm lying in the epidural space, estimated by the depth of the Tuohy needle when loss of resistance to saline or air injection was encountered. All were initiated with 0.5% bupivacaine 10 ml (3 ml test dose followed by 7 ml bolus), and maintained with a 0.08% bupivacaine infusion running at a rate of 20 ml/hour.

Pressure recordings were taken 1–2 hours after the test dose. The fetal heart rate trace was inspected for any signs of abnormality before measurements were started. Maternal arterial blood pressure was measured at one-minute intervals using an indirect method (Dinamap 1640-Criticon). A sterile disposable pressure dome was primed with 0.9% saline solution and connected to the epidural catheter via the three-way tap. Measurements were started after calibration of the transducer (Gould-Statham P23 ID), which was hand-held at the correct levels in order that all recordings should be referred to the same level. These were at the level of the lumbar spine for the lateral positions, and 5 cm above the bed surface at lumbar spine level for the supine and wedged supine positions (the mean depth of the epidural space from the skin at lumbar level is 5 cm). Recordings were made only between contractions, as indicated by the tocographic trace, to eliminate the effect of uterine contraction on epidural space pressure. The degree of cervical dilatation was assessed by a midwife immediately prior to the measurements, in case the second stage of labour was imminent.

The epidural pressures associated with a set sequence of maternal postures were recorded. Maternal heart rate and arterial blood pressure, along with fetal heart rate were recorded for each posture. Each posture was held for 60 seconds, to ensure a steady reading for each recorded value, and the sequence was as follows: 1, right lateral; 2, full supine; 3, supine with right buttock wedge; 4, supine with right buttock wedge and right uterine displacement; 5, left lateral; 6, supine with legs drawn up over abdomen; 7, supine with right buttock wedge.

Results

Figure 1 shows the mean epidural pressure associated with each posture in the sequence. The lowest pressures were associated with the right lateral and left lateral positions; the mean pressures were 1.2 kPa and 1.0 kPa respectively. The highest pressures were associated with the full supine (1.7 kPa), wedged supine (1.8 kPa) and supine with legs drawn up (1.9 kPa) postures.

There were statistically significant differences in the mean epidural pressures between the left lateral position and all of the supine positions except the wedged supine.

No significant alterations in maternal blood pressure or heart rate were recorded in any of the postures in the sequence.

All mean fetal heart rates remained within the normal range throughout the recordings, and the lowest recorded, at 95 and 102 beats/minute, were associated with the wedged supine with right uterine displacement posture.

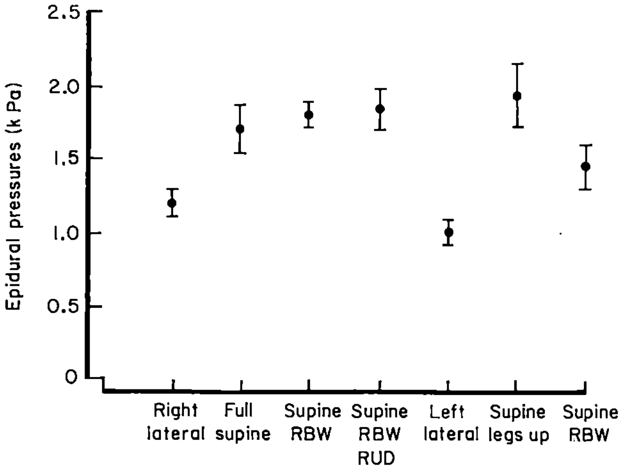


Fig. 1. Mean epidural pressures associated with each of the postures. Bars represent SEM. RBW, right buttock wedge; RUD, right uterine displacement.

Discussion

Clinical detection of aortocaval compression depends on the balance between the degree of obstruction and sympathetic nervous system compensation. Subclinical aortocaval compression may frequently occur and reduce uterine perfusion, unless great care is taken to keep the uterus shifted away from the aorta and inferior vena cava. Posture number 4 deserves special comment. It may be observed under other circumstances when an obstetrician or midwife is displacing the uterus to the right to ascertain fetal heart beat or position. It is a manipulation which needs to be brief.

This study shows that it is possible for an anaesthetist to use posturing of the patient to alter lumbar epidural space pressure. The adoption of any of the postures other than lateral or wedged supine results in a significant increase in epidural space pressure which is sustained. The magnitude of the increase in pressure, and its constant relation to the adoption of the supine position supports our hypothesis, that it is the degree of inferior caval compression which determines the epidural space pressure in the full term parturient. This finding is in agreement with that reported by Messih.[10] They do not provide conclusive proof, but the observed pressure changes support the hypothesis that a cephalad surge of CSF from the lumbar region is induced by certain changes of maternal posture.[11] The series of postures employed in this study were chosen to represent those which occur commonly in the labour ward and obstetric operating theatre, and have not been studied in previous work on this subject.

The increase in epidural space pressure seen in association with certain maternal postures is thought to be caused by engorgement of the epidural venous plexus, due to vena caval compression. It has been reported previously that inferior vena caval compression will increase lumbar epidural space pressure without affecting cervico-thoracic epidural space pressure.[12] This work demonstrated that on the basis of induced pressure changes, the extradural space could be regarded as three independent regions; cervicothoracic, lumbar and sacral. Epidural veins pass through the enclosed space of the spinal canal, and any alteration in the epidural venous pressure causes a directly transmitted change in CSF pressure.[13] It is possible that this increase in lumbar epidural space pressure, with consequent cephalad surge of CSF, could be the mechanism which causes posture-related variations in the level of sensory blockade after spinal anaesthesia.

In conclusion, changes in posture which involve an increase in inferior vena caval compression are likely to further the spread of free local anaesthetics in the subarachnoid space.

References

1. Carrie LE, O'Sullivan G. Subarachnoid bupivacaine 0.5% for caesarean section. *European Journal of Anaesthesiology* 1984; **1:** 275–83.
2. Sprague DH. Effects of position and uterine displacement on spinal anesthesia for cesarean section. *Anesthesiology* 1976; **44:** 164–6.
3. Barclay DL, Renegar OJ, Nelson EW, Jr. The influence of inferior vena cava compression on the level of spinal anesthesia. *American Journal of Obstetrics and Gynecology* 1968; **101:** 792–800.
4. Russell IF. Spinal anaesthesia for caesarean section. The use of 0.5% bupivacaine. *British Journal of Anaesthesia* 1983; **55:** 309–14.
5. Shah JL. Influence of cerebrospinal fluid on epidural pressure. *Anaesthesia* 1981; **36:** 627–31.
6. Loman J, Myerson A, Goldman D. Effects of alterations in posture on the cerebrospinal fluid pressure. *Archives of Neurology and Psychiatry* 1935; **33:** 1279–95.
7. Marx GF, Oka Y, Orkin LR. Cerebrospinal fluid pressures during labor. *American Journal of Obstetrics and Gynecology* 1962; **84:** 213–9.
8. Shah JL. Effect of posture on extradural pressure. *British Journal of Anaesthesia* 1984; **56:** 1373–7.
9. Galbert MW, Marx GF. Extradural pressures in the parturient patient. *Anesthesiology* 1974; **40:** 499–502.
10. Messih MNA. Epidural space pressures during pregnancy. *Anaesthesia* 1981; **36:** 775–82.
11. Tunstall ME, Ostheimer GW. Obstetrics. In: Nunn JF, Utting JE, Brown BR, eds. *General anaesthesia, 5th edn.* London: Butterworths, 1989: 988–1008.
12. Usubiaga JE, Moya F, Usubiaga LE. Effect of thoracic and abdominal pressure changes on the epidural space pressure. *British Journal of Anaesthesia.* 1967; **39:** 612–8.
13. Pollock LJ, Boshes B. Cerebrospinal fluid pressure. *Archives of Neurology and Psychiatry* 1936; **36:** 931–94.

Anaesthesia, 1989, Volume 44, pages 753–757

A comparison between propofol and thiopentone as induction agents in obstetric anaesthesia

J. MOORE, K. M. BILL, R. J. FLYNN, K. T. McKEATING AND P. J. HOWARD

Summary

Two comparable series of 21 patients who had elective Caesarean section had general anaesthesia induced by thiopentone sodium 4.53 (SD 0.65) mg/kg or propofol 2.15 (SD 0.26) mg/kg. Maintenance was similar for both groups. Blood pressure was lower in the propofol group during the induction–delivery interval. Umbilical/maternal vein ratios for thiopentone and propofol were 8.5 and 7.2 respectively. Infant wellbeing as judged by Apgar score and cord blood analysis showed little difference between the two induction agents. Factors associated with uterine relaxation and bleeding were similar in the two groups.

Key words

Anaesthesia; obstetric.
Anaesthetics intravenous; thiopentone sodium, propofol.

Thiopentone sodium has been used in obstetric anaesthesia since 1936[1] and is regarded as the standard induction agent. Early investigators used larger doses and Hellman *et al.*[2] showed that considerable quantities were transferred to the infant. It was later demonstrated[3] that placental transfer occurred within seconds and that repeated injection caused significant infant depression.[4] Present-day opinion is that a single dose of 3–5 mg/kg[5,6] should be given to induce sleep and that maintenance of anaesthesia before delivery should be by inhalation agents.

Propofol, diisopropyl phenol, has properties which suggest that it might be a useful alternative to thiopentone. The suspension has a pH of 7.0 which makes it less likely to cause local tissue or vascular complications. The cardiovascular response to tracheal intubation is less than with thiopentone.[7] Propofol is more rapidly metabolised and excreted than the barbiturate, and hangover after anaesthetic is reduced.[8]

This investigation reports a comparison of propofol and thiopentone used as induction agents for general anaesthesia for patients who have elective Caesarean section. It had the approval of the Local Medical Research Ethics Committee and verbal consent from all patients.

Materials and methods

Women selected were healthy and had a pregnancy of at least 36 weeks' gestation with a single uncompromised fetus. Elective Caesarean section was for disproportion or abnormal fetal presentation. Oral ranitidine 150 mg was given 90 to 120 minutes before anaesthesia and left lateral tilt, instituted 15 minutes before induction, was maintained until delivery. Two intravenous cannulae were introduced, one in the right arm for the infusion of a compound sodium lactate solution and the other in the left arm for blood sampling. The ECG, blood pressure automatically by Dinamap recorder, and tissue oxygen saturation by pulse oximeter, were monitored before and during anaesthesia. Ventilation of the lungs during anaesthesia was adjusted to maintain an end-tidal carbon dioxide of 4 to 4.25 kPa using a Datex Normocap. All patients were preoxygenated with 100% oxygen for 5 minutes before induction, and cricoid pressure was applied from the start of injection of the induction agent until tracheal anaesthesia was established.

Women were randomly allocated to receive either 2.5% thiopentone sodium or 1% propofol; the total dose was that required to abolish the eyelash reflex. Suxamethonium 100 mg was given to facilitate tracheal intubation and maintenance was by inhalation of 50% nitrous oxide in oxygen, supplemented by 0.75% isoflurane until skin closure. The nitrous oxide concentration was increased to 67% after delivery and intravenous fentanyl 0.1 mg was given. Muscle relaxation was continued with vecuronium 4 mg and further 2-mg increments were given if required. Syntocinon 5 units was given intravenously at delivery, and

---

J. Moore, MD, PhD, FFARCS, Consultant, K.M. Bill, MB, FFARCS, Senior Tutor, R.J. Flynn, MB, FFARCS, K.T. McKeating, MB, FFARCS, Senior Registrars, P.J. Howard, FIScT, Senior Technician, Department of Anaesthetics, The Queen's University of Belfast, Whitla Medical Building, 97 Lisburn Road, Belfast BT9 7BL.

Accepted 27 February 1989.

0003–2409/89/090753+05 $03.00/0

© 1989 The Association of Anaesthetists of Gt Britain and Ireland

further doses of a similar amount were administered if indicated by uterine relaxation or bleeding. Residual myoneural block was reversed in all patients by glycopyrronium 0.5 mg and neostigmine 2.5 mg.

The following observations were made. The total dose of thiopentone sodium and propofol was noted, together with the times for the induction–delivery (ID), uterine–incision delivery (UI) intervals and total duration of anaesthesia. Blood pressure and heart rate were recorded at 1-minute intervals for 3 minutes before induction, throughout the ID period and at 5-minute intervals thereafter. The infant's 1- and 5-minute Apgar scores and the method of resuscitation was noted. The number of doses of Syntocinon was recorded. The surgeon, unaware of the induction agent used, assessed uterine contractility and bleeding by visual analogue score; 0 was severe relaxation and 10, marked contraction. Each patient had haemoglobin and haematocrit estimations before and at 24 hours after surgery. Maternal arterial, umbilical venous and arterial heparinised blood samples (the latter from a double clamped loop of cord) were collected at delivery for pH, $P\text{O}_2$ and $P\text{CO}_2$ measurement using a Corning pH blood gas analyser. Additional delivery samples of maternal and umbilical venous blood were placed in lithium heparin tubes for determination of plasma thiopentone and whole blood propofol levels. The barbiturate sample was centrifuged and both the supernatant plasma and propofol blood were stored at −20°C until analysis. Levels of both drugs were measured by high pressure liquid chromatography using a modification of the method described by Plummer[9] for propofol and by Howard and Toner[10] for thiopentone.

Recovery was timed from the end of anaesthesia until spontaneous rejection of the tracheal tube. Immediate sickness and need for analgesic treatment during the first hour after anaesthetic was recorded. All patients were visited at 24 hours to ascertain if late anaesthetic dreaming or awareness had occurred.

Results are presented as the mean (SD) unless otherwise stated. Statistical evaluation was performed using the unpaired Student's *t*-test and Chi-squared analysis; $p < 0.05$ was considered to be significant.

Results

Forty-two patients were included: 21 received thiopentone and 21 propofol. Their physical and obstetric characteristics were comparable (Table 1). The mean (SD) ID, UD and duration of anaesthesia (minutes) were 14.1 (2.9), 2.4 (1.1) and 50.3 (17.5) for thiopentone and 11.9 (4.2), 2.3 (1.0) and 48.4 (14.3) for propofol. None of the differences was statistically significant. The total induction dose for thiopentone was 333 (56.1) mg and for propofol 168 (25.5) mg, which, expressed in mg/kg, was 4.53 (0.68) and 2.15 (0.26) respectively.

Table 1. Mean (SD) physical and obstetric characteristics.

Induction agent (*n*)	Age (years)	Weight (kg)	Parity	Gestation (weeks)
Thiopentone (21)	29.4 (5.8)	74.5 (13.1)	2.0 (1.1)	38.1 (0.9)
Propofol (21)	32.3 (6.3)	78.7 (12.5)	1.5 (0.8)	38.2 (0.6)

The percentage variation in the 1-minute recordings of systolic, diastolic, mean blood pressure and pulse rate during the ID interval from the mean of the three pre-induction readings are shown in Figure 1. The general trend was for all blood pressure values to be lower in the propofol group. However, statistical comparison of the absolute values showed that while the pre-induction values of both groups were comparable, the 3-, 4- and 5-minute systolic and 4-minute diastolic readings in the propofol series were significantly lower ($p < 0.05$). Out of a total 256 systolic readings in the thiopentone group and 221 in the propofol group, 15 and 27 respectively were below 100 mmHg during the ID interval. This was significant (Chi-squared 5.21; df 1; $p < 0.05$). One patient given propofol had a marked hypotensive episode before delivery which did not respond to increased infusion rate and further uterine displacement. Ephedrine 10 mg intravenously reversed the hypotension. The infant had Apgar scores of 4 and 9 at 1 and 5 minutes and an umbilical vein pH of 7.30 and $P\text{O}_2$ of 2.7 kPa.

The maintenance of anaesthesia and muscle relaxation were similar for both induction agents. Additional increments of vecuronium were not required and re-establishment of adequate spontaneous ventilation after reversal drugs was without problems in either series. Spontaneous rejection of the tracheal tube occurred in 3.2 (1.8) minutes and 4.4 (1.7) minutes in the propofol and thiopentone series respectively. Four patients vomited during emergence from thiopentone-induced anaesthesia as compared to none in the propofol series. Twelve women from each group required analgesic treatment during the first post-operative hour. One woman given thiopentone reported vague recall at 24 hours of induction and intubation.

The factors associated with blood loss and uterine contractility are shown in Table 2 and did not show significant variation with the induction agent used. Two patients required blood transfusion towards the end of operation: one given thiopentone had an undiagnosed type 4 placenta praevia and the other in the propofol group had marked adhesions from a previous Caesarean section.

Table 2. Factors associated with blood loss.

Induction agent (*n*)	Blood transfusion	Mean (SD) haemoglobin and haematocrit (g/dl)				VAS assessment (mm)	Repeated Syntocinon
		Before	After	Before	After		
Thiopentone (21)	1	11.9 (1.1)	11.5 (1.3)	0.36	0.35	5.6 (1.7)	1
Propofol (21)	1	12.1 (0.9)	11.4 (1.0)	0.36	0.34	5.2 (1.7)	1

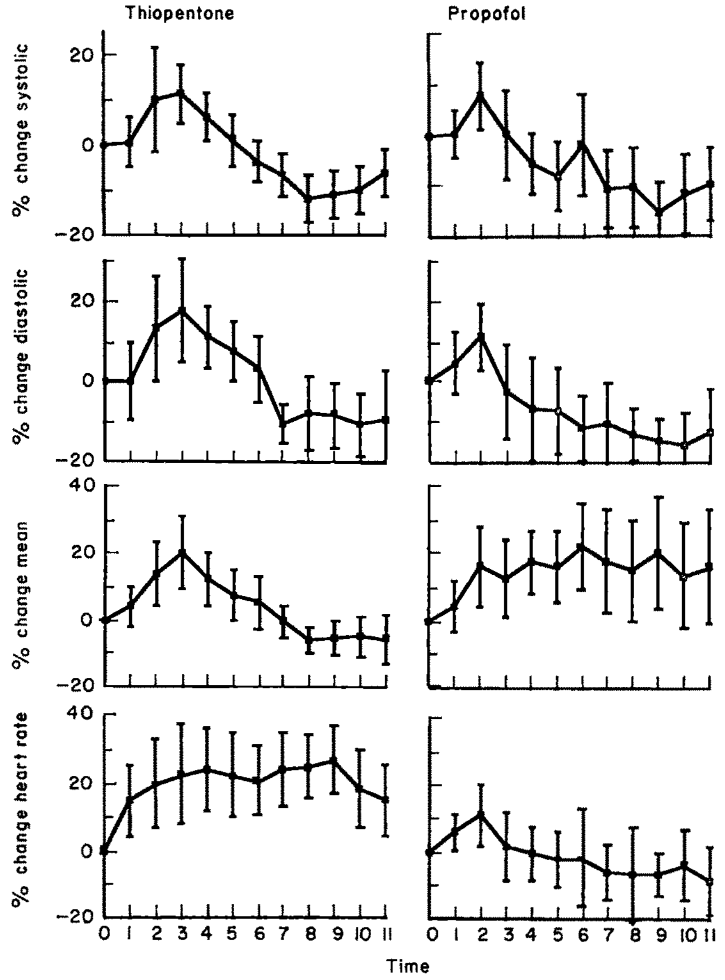


Fig. 1. Variations in systolic, diastolic and mean blood pressure and heart rate, with 95% confidence limits, after thiopentone and propofol induction during the initial 10 minutes of anaesthesia.

The average Apgar scores (range) at 1 and 5 minutes were 7.1 (5 to 9) and 8.9 (8 to 10) for thiopentone and 7.2 (4 to 9) and 9.1 (8 to 10) for propofol. No infant required tracheal resuscitation or drug therapy other than oxygen by mask. Two infants were transferred to the ICU, one in the thiopentone series because of distressed respiration which did not require ventilation and the other from the propofol group for twitching at 3 days after delivery. Both were discharged home at 7 days.

The maternal arterial and umbilical venous and arterial pH, Po_2 and Pco_2 at delivery are shown in Table 3. None of the variations was statistically significant.

The maternal and umbilical venous plasma levels at delivery for the two induction agents are shown in Figure 2; the mean (SD) value for thiopentone was 4.67 (1.50) mg/litre and 3.63 (1.18) mg/litre, and for propofol 0.93 (0.56) mg/litre and 0.59 (0.35) mg/litre respectively. The UV/MV ratio was 0.85 (0.43) for thiopentone and 0.72 (0.38) for propofol. Three of the umbilical vein levels in the thiopentone group exceeded the maternal venous level as compared to four in the propofol series.

Discussion

Properties of the ideal induction agent for obstetric use should include sleep in one arm–brain circulation time, minimal cardiovascular upset and no excitatory movement. Rapid injection of a predicted bolus dose of thiopentone in the range of 3 to 5 mg/kg followed by a large dose of suxamethonium has been recommended.[5,6] The induction agent was titrated against patient response in our study: the end point was the loss of eyelash reflex, and resulted in the dose of thiopentone being in the upper part of the accepted range. Grounds *et al.*[11] compared the onset of anaesthesia with thiopentone and propofol given intravenously over 20 seconds during a period of reactive hyperaemia after temporary occlusion of forearm blood flow, and calculated a relative potency for thiopentone to propofol of 1 to 1.6, as compared to 1 to 2 in this study. It was shown in a dose-response study[12] that 2.25 to 2.5 mg/kg propofol administered in 20 seconds was a reliable induction agent in

Table 3. pH, Po_2 and Pco_2 in maternal arterial (MA) and umbilical venous (UV) and arterial (UA) blood at delivery.

Induction agent (*n*)	Sample	pH	Po_2 kPa	Pco_2 kPa
Thiopentone (21)	MA	7.39 (0.05)	25.60 (8.57)	4.57 (0.69)
	UV	7.33 (0.03)	5.14 (1.35)	6.28 (0.96)
	UA	7.27 (0.03)	2.79 (0.53)	7.39 (1.27)
Propofol (21)	MA	7.38 (0.04)	23.60 (6.89)	4.53 (0.67)
	UV	7.30 (0.08)	5.30 (1.97)	6.12 (0.94)
	UA	7.27 (0.10)	3.08 (1.18)	7.28 (0.84)

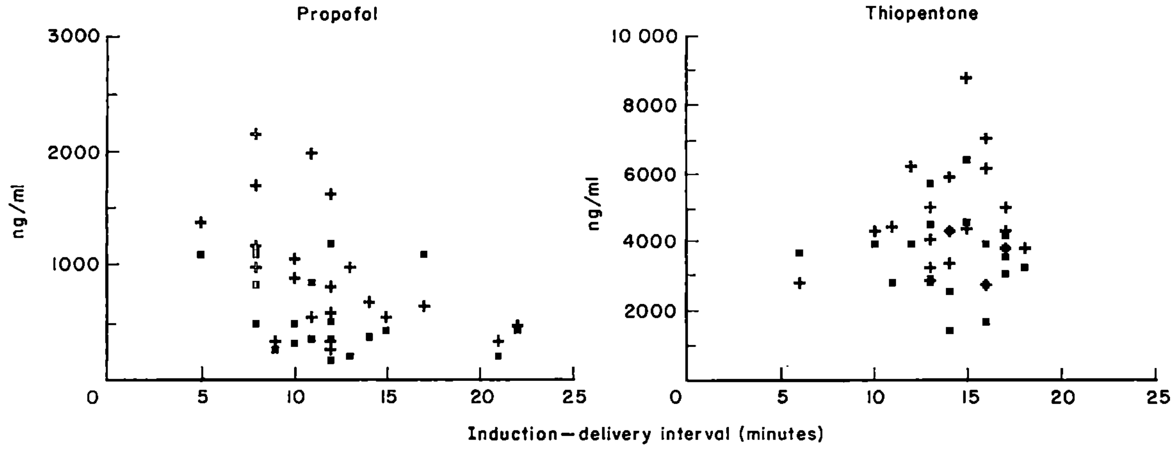


Fig. 2. Plasma thiopentone and blood propofol levels in maternal (+) and umbilical (■) vein samples at delivery.

younger patients. The results of our investigation indicate that this dose is suitable for the parturient. Excitatory effects were not seen with either induction agent and movement at tracheal intubation did not occur.

A hypertensive response to tracheal intubation[13] is common in the lightly anaesthetised obstetric patient and could be important if hypertension or an intracranial vascular lesion are present. In nonobstetric use propofol was shown to attenuate the increase in arterial pressure and heart rate associated with laryngoscopy and intubation.[7] Increases in systolic, diastolic and mean blood pressures reported here were less with propofol. However, episodes of hypotension, as defined by a systolic blood pressure below 100 mmHg during the ID interval, were significantly less after thiopentone. Significant hypotension in an investigation such as this is difficult to define. James *et al.*[14] stated that in unpremedicated parturients pre-operative stress leads to abnormally high comparative pretreatment blood pressure, and that in some patients systolic readings below 100 mmHg are the norm. Therefore, if these criteria are used to assess the incidence, hypotension is abnormally frequent. However, one patient given propofol had hypotension which responded to a vasopressor. The effect of rate of injection was not evaluated and in clinical use propofol might be injected more rapidly than in this study. However, two investigations[15,16] have shown that haemodynamic effects are minimally changed by rate of injection.

The maternal pH, $P\text{O}_2$ and $P\text{CO}_2$ readings were very similar for the two groups so that variations in these values for umbilical vein and artery blood reflect differences in placental or infant tissue perfusion. None of these indicated that there was greater impairment with propofol compared with that after thiopentone. The average 1-minute Apgar scores showed no difference between the induction agents. The one infant who scored 4 was that of the mother with the resistant hypotension, but the umbilical vein pH value was satisfactory. All neonates were well at 5 minutes. The transfer of two infants to the intensive care unit was considered not to be associated with the induction agent used.

Plasma thiopentone[17] and blood propofol levels associated with loss of consciousness were reported as 39.4 (2.5) μg/ml and up to 6.38 μg/ml respectively. Recovery of consciousness with propofol is associated with blood levels between 1.0 and 2.19 μg/ml.[18] The maternal levels at delivery for either induction agent are well below that required to guarantee unconsciousness. Both agents are readily transferred to the infant and there was no correlation in either series between levels in the umbilical vein, the ID interval or the 1-minute Apgar score of the infant. The UV/MV ratio showed considerable variation in both groups; the range for thiopentone was 0.4 to 2.0 and for propofol 0.2 to 1.7. In three of the thiopentone series and four of the propofol group the UV/MV ratio exceeded 1.0. This finding is common to many investigations on thiopentone–placental transfer[2,4,19] and probably indicates more rapid distribution and metabolism of the induction agent in the mother than in her infant.

The other findings showed that, as compared to thiopentone, propofol did not affect uterine contractility or bleeding, the dosage of muscle relaxants or the need for immediate analgesia after operation. Recovery was marginally more rapid with propofol, but this is of little clinical significance.

This investigation shows that propofol, in a dose of 2.0 to 2.5 mg/kg is an acceptable alternative to thiopentone for the induction of general anaesthesia in obstetrics. Pre-existing hypertension may be an indication for its use.

Acknowledgments

The authors express their thanks to the medical and nursing staff of Jubilee Maternity and Craigavon Area Hospitals for their cooperation and help.

References

1. Solomons EB. Pentothal sodium in obstetrics. *Irish Journal of Medical Science* 1936; **132:** 746–51.
2. Hellman LM, Shettles LB, Manahan CP, Eastman NJ. Sodium pentothal anesthesia in obstetrics. *American Journal of Obstetrics and Gynecology* 1944; **48:** 851–60.
3. Kosaka Y, Takahashi T, Mark LC. Intravenous thiobarbiturate anesthesia for cesarean section. *Anesthesiology* 1969; **31:** 489–506.
4. Finster M, Mark LC, Morishima HO, Moya F, Perel J, James LS, Dayton PG. Plasma thiopental concentrations in the newborn following delivery under thiopentone-nitrous oxide anesthesia. *American Journal of Obstetrics and Gynecology* 1966; **95:** 621–9.
5. Crawford JS. *Current reviews in obstetrics and gynaecology. 1. Obstetric analgesia and anaesthesia.* Edinburgh: Churchill Livingstone, 1982; 95.
6. Moir DD, Thorburn J. *Obstetric anaesthesia and analgesia,* 2nd edn. London: Baillière Tindall, 1986: 182.

7. Coates DP, Monk CR, Prys-Roberts C, Turtle M, Norley I, Spelina KR. Haemodynamic responses to induction and endotracheal intubation with propofol/nitrous oxide anaesthesia in humans. *European Journal of Anaesthesia* 1986; **3:** 65–6.
8. Kay NH, Sear JW, Uppington J, Cockshott ID, Douglas EJ. Disposition of propofol in patients undergoing surgery. A comparison in men and women. *British Journal of Anaesthesia* 1986; **58:** 1075–9.
9. Plummer GF. Improved method for the determination of propofol in blood by high-performance liquid chromatography with fluorescence detection. *Journal of Chromatology Biomedical Applications* 1987; **421:** 171–6.
10. Howard PJ, Toner W. Measurement of thiopentone in biological materials. Appendix 3. In: Dundee JW, Wyant GM, eds. *Intravenous anaesthesia,* 2nd edn. London: Churchill Livingstone, 1987.
11. Grounds RM, Moore M, Morgan M. The relative potencies of thiopentone and propofol. *European Journal of Anaesthesia* 1986; **3:** 11–17.
12. Dundee JW, Robinson FP, McCollum JSC, Patterson CC. Sensitivity to propofol in the elderly. *Anaesthesia* 1986; **41:** 482–5.
13. Loughran PG, Moore J, Dundee JW. Maternal stress response associated with caesarean delivery under general and epidural anaesthesia. *British Journal of Obstetrics and Gynaecology* 1986; **93:** 943–9.
14. James CF, Gibbs CP, Gravenstein JS, Van der Aa J. Maternal hypotension: are current criteria valid? *Anesthesiology* 1982; **57** (Suppl.): A393.
15. Coursange F, Aubert M. The effect of injection speed on arterial blood pressure and heart rate with propofol. *Annales Françaises d'anésthésie et de Réanimation* 1987; **6:** 258–60.
16. Rolly G, Versichelen L, Huyghe L, Mungroop H. Effect of speed of injection on induction of anaesthesia using propofol. *British Journal of Anaesthesia* 1985; **57:** 743–6.
17. Becker KE. Plasma levels of thiopental necessary for anesthesia. *Anesthesiology* 1978; **49:** 192–6.
18. Schuttler J, Stoeckel H, Schwilden H. Pharmacokinetic and pharmacodynamic modelling of propofol (Diprivan) in volunteers and surgical patients. *Postgraduate Medical Journal* 1985; **61** (Suppl. 3): 53–4.
19. Morgan DJ, Blackman GL, Paull JD, Wolf LJ. Pharmacokinetics and plasma binding of thiopental. II: Studies at cesarean section. *Anesthesiology* 1981; **54:** 474–80.

Anaesthesia, 1989, Volume 44, pages 758–762

Comparison of propofol and thiopentone for induction of anaesthesia for elective Caesarean section

M. VALTONEN, J. KANTO AND P. ROSENBERG

Summary

Propofol 2.5 mg/kg was compared with thiopentone 5 mg/kg as an induction agent for elective Caesarean section. Thirty-two healthy women with cephalopelvic disproportion were included in an open randomised study. The placental transfer of propofol was also studied in 10 other mothers given a single dose of 2.5 mg/kg. The induction characteristics and haemodynamic response to propofol and thiopentone were similar. Side effects were rare with both agents, but propofol caused more discomfort on injection compared to thiopentone. Recovery times were shorter after propofol as evaluated by time to orientation, recovery scoring after anaesthesia and measurements with the Maddox wing. Rapid placental transfer and significant fetal uptake were detected for propofol. There was no significant neonatal depression as assessed by Apgar scores and blood gas analyses. Propofol appears to be a suitable alternative to thiopentone as an induction agent for anaesthesia in elective Caesarean section.

Key words

Anaesthetics, intravenous; propofol, thiopentone.
Anaesthesia, obstetric.

Regurgitation of gastric contents associated with aspiration is a well-known risk at induction of general anaesthesia for Caesarean section because of slow gastric emptying during late pregnancy.[1] Another problem is to minimise drug effects on the fetus, yet avoid the mother's intra-operative awareness. Induction must therefore be smooth and rapid to ensure unconsciousness for the manoeuvres necessary prior to introduction of inhalational agents, but with no residual effect on the neonate at the time of delivery.[2]

Thiopentone has been the routine induction agent of anaesthesia for Caesarean section since the 1930s because of its rapid and predictable action. However, it can also cause marked decreases in arterial blood pressure, and this, together with the rapid placental transfer, may induce some depression of the fetus. Today there are few alternatives to thiopentone. Thus midazolam has been shown to have a great variability of action when used to induce anaesthesia[2,3] while etomidate causes adrenocortical suppression[4,5] which has also been shown to occur in the neonate after elective Caesarean section.[6]

We compared propofol with thiopentone for induction of anaesthesia in elective Caesarean section in the present study. Particular attention was paid to induction characteristics and the neonatal effects of both agents.

Methods

Thirty-two healthy women who had elective Caesarean section because of cephalopelvic disproportion and with no other complications of pregnancy (duration $>$ 38 weeks) were included in an open, randomised study. The study was approved by the Hospital Ethics Committee, and informed consent was obtained from each mother. Their characteristics are given in Table 1.

The mothers fasted overnight and were unpremedicated. They were placed on the operating table in the left lateral tilt position and a cannula was inserted into a vein of the forearm. 500–1000 ml lactated Ringer's solution was infused during the operation. Anaesthesia was induced intravenously after pre-oxygenation, with either propofol 2.5 mg/kg or thiopentone 5.0 mg/kg followed by suxamethonium 1 mg/kg to facilitate tracheal intubation. Sixty percent nitrous oxide in oxygen and isoflurane 0.7% were used from the beginning of anaesthesia to the clamping of the umbilical cord. Anaesthesia was maintained after that with 70% nitrous oxide in oxygen, and isoflurane was discontinued. Vecuronium 0.10–0.12 mg/kg was used for muscle relaxation, and buprenorphine 0.004 mg/kg to provide analgesia during surgery. Droperidol 0.018 mg/kg,

---

M. Valtonen, MD, Resident in Anaesthesiology, J. Kanto, MD, Reader in Anaesthesia and Clinical Pharmacology, Department of Anaesthesiology, University of Turku, P. Rosenberg, MD, Reader in Anaesthesia, Department of Anaesthesiology, University of Helsinki, Helsinki, Finland.

Accepted 30 January.

0003–2409/89/090758+05 $03.00/0

© 1989 The Association of Anaesthetists of Gt Britain and Ireland

Table 1. Patient characteristics, mean (SD).

	Propofol (n = 16)	Thiopentone (n = 16)
Age, years	27.4 (2.85)	30.5 (5.46)
Weight, kg	79.1 (8.94)	75.9 (8.87)
Height, cm	166.0 (5.98)	166.5 (6.14)
Primiparous, *n*	6	4
Previous Caesarean section, *n*	7	6

Table 2. Induction time, time from induction to uterine incision (I–I time) and time from uterine incision to cord clamping (I–C time) in both groups, mean (SD).

	Propofol (n = 16)	Thiopentone (n = 16)
Induction time, seconds	27.3 (4.3)	32.4 (10.4)
I–I time, minutes	4.4 (0.8)	4.4 (1.1)
I–C time, seconds	46.1 (14.0)	49.6 (25.4)

as an antiemetic agent, and oxytocin 5 IU were also administered after delivery. Glycopyrronium 0.01 mg/kg and neostigmine 0.05 mg/kg were used to reverse residual neuromuscular block.

The induction agent was injected as a single bolus during 10 seconds, and the induction time, taken as the time from the start of the injection to abolition of eyelash reflex, was recorded. The occurrence of any side effects at induction or during maintenance of anaesthesia was noted. The anaesthetists (J.K. and M.V.) assessed the quality of induction and maintenance of anaesthesia as good, adequate or poor.

Systolic and diastolic arterial pressures and heart rate were measured indirectly (Cardiocap, Datex Co.), before and after insertion of the cannula, immediately after injection of the induction agent, after tracheal intubation, after the beginning of surgery and thereafter at 5-minute intervals throughout the procedure. The end-tidal carbon dioxide ($P_{E'}CO_2$) was monitored continuously (Cardiocap) and the ventilation variables were adjusted to maintain the $P_{E'}CO_2$ at 4.5–5.5 kPa. The ECG was displayed continuously and neuromuscular block was monitored using a Datex Relaxograph.

Neonatal assessments included Apgar scores at 1, 5 and 15 minutes and neonatal weights; blood gas tensions and pH were measured from the umbilical vein and artery (178 pH-blood gas analyser, Corning). Samples were taken immediately after birth from a double-clamped section of the cord and analysed within 5 minutes. The time from induction of anaesthesia to uterine incision, from uterine incision to clamping of umbilical cord and from induction to blood sampling were recorded. The duration of the whole operation was also noted.

The completeness of recovery was assessed by using the critical flicker fusion frequency (CFF),[7] a Maddox wing apparatus[8] and the visual analogue scale (VAS) (subjective sedation).[9] These measurements were made before the induction of anaesthesia and at 15, 30, 45, 60, 90 and 120 minutes after orientation, which was taken as the time when the patients could recall their date of birth. In addition a scoring system to assess the patient's awakeness (2, fully awake; 1, rousable; 0, not responding), ventilation (2, is able to cough; 1, breathing easily; 0, airway requires attention) and movement (2, moving purposefully; 1, moving involuntarily; 0, not moving) was used at 3, 15, 30 and 180 minutes after orientation. A fully recovered patient therefore had a score of six.

The placental transfer of propofol was studied with 10 other patients [age 22–38 years (mean 28.5); weight 62–103 kg (mean 77.0); five primiparous and five multiparous]. Anaesthesia was induced with propofol 2.5 mg/kg injected over 10 seconds, and maintained as above. The propofol concentration in maternal venous blood (MV), in umbilical venous (UV) and arterial (UA) blood was determined by a high-performance liquid chromatographic method.[10] This method has a lower limit of sensitivity of approximately 2 ng/ml, and intra-assay coefficient of variation was about 5%.

Data are presented as mean (SD). Mean arterial pressure (MAP) was calculated as $\frac{1}{3}$ × (systolic + 2 × diastolic pressures). The statistical analysis was performed using two-way ANOVA (repeated measures on two factors) followed by the Newman–Keuls test.[11] Differences between groups were analysed with Student's *t*-test for parametric data and Fisher's exact test for nonparametric data. Scored data were analysed with the Mann–Whitney *U* test. A level of 0.05 was considered statistically significant.

Results

The groups were comparable for age, weight, height and pregnancy characteristics (Table 1). The induction characteristics for propofol and thiopentone were similar, and the onset of anaesthesia was rapid with both agents [propofol 27.3 seconds (4.3); thiopentone 32.4 seconds (10.4)] (Table 2). The quality of induction did not differ between the groups, and side effects were rare (Table 3). However, propofol caused significantly more discomfort on injection compared to thiopentone (6 versus 1, $p = 0.042$).

There were no significant differences in haemodynamic response between the groups during the induction and maintenance of anaesthesia (Fig. 1). Compared with the baseline values, the mean arterial pressure was stable after induction and increased 18–29% ($p < 0.01$) after tracheal intubation. The heart rate increased from the baseline values by 18–21% after induction and by 26–30% after intubation ($p < 0.01$), Figure 1. The duration of the procedure did not differ between the propofol and thiopentone groups [45.0 minutes (11.1) for propofol and 46.9 minutes

Table 3. Assessment of the quality of induction and numbers of patients with side effects during induction and recovery.

	Propofol (n = 16)	Thiopentone (n = 16)
Assessment by anaesthetists (*n*)		
Good	11	8
Adequate	5	8
Poor	0	0
Side effects (*n*)		
Induction:		
excitation	4	6
discomfort on injection	6	1*
Recovery:		
respiratory upset	2	3
vomiting	0	2
flush	0	1
restlessness	2	0
headache	1	0

*p = 0.042 (Fisher's exact test).

Table 4. Duration of anaesthesia and recovery time from the end of anaesthesia to opening eyes on command and time from opening eyes to orientation in both groups, mean (SD).

	Propofol ($n = 16$)	Thiopentone ($n = 16$)
Duration of anaesthesia, minutes	45.0 (11.1)	46.9 (17.6)
Time to opening of the eyes, minutes	3.2 (2.9)	5.0 (7.5)
Time to orientation, minutes	1.0 (0.9)	2.3 (1.0)*

*p = 0.0011 (Student's *t*-test).

(17.6) for thiopentone]. The recovery times from the end of the procedure to opening eyes on command did not differ statistically between the groups, but the time to orientation was significantly shorter after propofol (p = 0.0011; Table 4).

The recovery scoring after anaesthesia also showed a significant difference between the groups at 3, 15 and 30 minutes (Table 5). The recovery results measured with VAS and CFF did not reach statistical difference, but measurements with the Maddox wing apparatus indicated shorter recovery times after propofol than after thiopentone at 30, 45 and 60 minutes after orientation (Fig. 2).

The incidence of side effects during recovery did not differ between the groups (Table 3). None of the patients reported any awareness during anaesthesia and all found the course of anaesthesia acceptable.

The Apgar scores of the neonates did not differ significantly (Table 6). The weights (Table 6) and the blood gas analyses (Table 7) of the neonates were also comparable and within the normal range.

Table 5. Recovery scores concerning the patients' awakeness, ventilation and movements (maximum total score 6) at 3, 15, 30 and 180 minutes after the orientation of patients in both groups, mean (SD).

	Propofol ($n = 16$)	Thiopentone ($n = 16$)
Recovery scores (0–6)		
3 minutes after orientation	3.88 (1.15)	3.00 (0.73)*
15 minutes after orientation	5.38 (0.89)	4.12 (1.15)**
30 minutes after orientation	5.81 (0.41)	4.87 (0.88)***
180 minutes after orientation	6.00 (0.00)	5.75 (0.45)ns

* p = 0.035
** p = 0.0039
*** p = 0.0026
ns, not significant (Mann–Whitney *U* test).

The propofol concentrations in maternal venous blood and in umbilical venous and arterial blood are presented in Table 8. The concentration in MV was slightly higher than in UV [2.70 μg/ml (0.43) versus 2.26 μg/ml (0.52)] and significantly higher than in UA [1.80 μg/ml (0.36) p = 0.0001]. The concentration in UV was also significantly higher than in UA (p = 0.030).

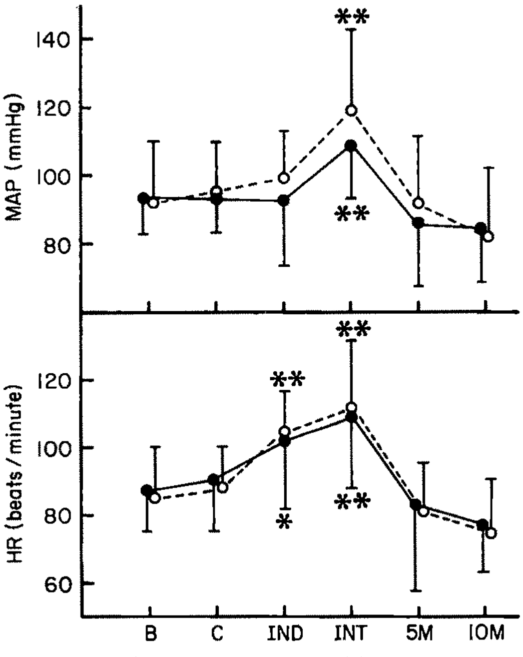


Fig. 1. Mean arterial pressure (MAP) and heart rate (HR) before induction of anaesthesia (B), after insertion of the cannula (C), immediately after injection of the induction agent (IND), immediately after intubation (INT) and 5 minutes (5M) and 10 minutes (10M) after the induction of anaesthesia in propofol (●) and thiopentone (○) groups. Mean SD, repeated measures ANOVA followed by Newman–Keuls test. * = $p < 0.05$ and ** = $p < 0.01$ compared to the baseline value (B).

Discussion

Elective Caesarean section is usually performed with epidural or general anaesthesia. It is clinically important, when the latter is used, that the anaesthetic agent provides stable conditions while limiting intra-operative recall. The

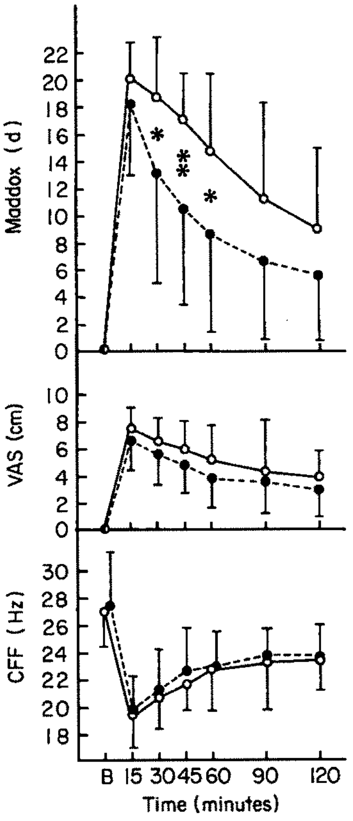


Fig. 2. Completeness of recovery assessed by Maddox wing (Maddox), visual analogue scale (VAS) and critical flicker fusion (CFF) as a function of time in propofol (●) and thiopentone (○) groups. Mean SD, repeated measures ANOVA followed by Newman–Keuls test. * = $p < 0.05$ and ** = $p < 0.01$ compared between the groups.

Table 6. Neonatal weights, mean (SD) and Apgar scores (median and range) at 1, 5 and 15 minutes after delivery.

	Propofol ($n=16$)	Thiopentone ($n=16$)
Neonatal weights g	3224.4 (539.1)	3510.6 (664.0)
Apgar scores (0–10):		
at 1 minute	9 (6–10)	9 (7–10)
at 5 minutes	9 (8–10)	9 (8–10)
at 15 minutes	9 (8–10)	9 (8–10)

number of patients in the present study was small, but none reported awareness during the procedure. Nor was any significant cardiovascular depression found after induction of anaesthesia with propofol or thiopentone. The induction characteristics were good with both agents, but discomfort on injection was a frequent finding (37.5%) in the propofol group. However, this fact did not affect the patients' acceptance of propofol as an induction agent. It has been shown that injection into a large vein or the mixing of lignocaine with propofol decreases the incidence of this discomfort.[12–15] Some excitation was also found during induction with both agents.

The measurements carried out with Maddox wing and the recovery scores indicated shorter recovery times after propofol than thiopentone. In addition, the time from opening eyes after anaesthesia to patients' orientation showed a statistically significant difference in favour of propofol. This offers a significant advantage when recovery room capacity is limited, and patients often subjectively report rapid recovery. The CFF and VAS were both less sensitive in the detection of the differences between the two drug effects as compared to Maddox wing. This finding also agrees with some previous studies.[8,16,17]

A rapid and reliable intravenous anaesthetic agent should rapidly cross the blood/brain barrier, and this feature is usually followed by rapid placental transfer.[18,19] Propofol is a very lipophilic undissociated agent with a low molecular weight, and the placental transfer of propofol apparently depends on placental blood flow and the concentration gradient between the mother and fetus. Thus, the induction dose of propofol and the time from induction of anaesthesia to clamping of umbilical cord probably have important effects on the concentration of propofol in the fetus.

Table 7. Blood gas tensions and pH samples of umbilical vein and artery (178 pH-blood gas analyser, Corning) and time from the beginning of anaesthesia to obtaining the blood samples, mean (SD).

	Propofol ($n=16$)	Thiopentone ($n=16$)
Umbilical vein		
pH	7.37 (0.044)	7.35 (0.037)
$P\text{CO}_2$ (kPa)	5.44 (1.21)	5.47 (0.82)
$P\text{O}_2$ (kPa)	5.10 (1.62)	4.39 (1.14)
Standard bicarbonate (mmol/litre)	22.4 (2.5)	21.4 (2.0)
Base excess (mmol/litre)	−2.0 (1.2)	−2.6 (1.9)
Umbilical artery		
pH	7.32 (0.038)	7.31 (0.041)
$P\text{CO}_2$ (kPa)	6.46 (0.89)	6.79 (1.30)
$P\text{O}_2$ (kPa)	3.14 (1.23)	2.90 (0.88)
Standard bicarbonate (mmol/litre)	21.9 (1.2)	20.8 (1.7)
Base excess (mmol/litre)	−1.7 (1.0)	−2.6 (2.1)
Time of blood samples, minutes	5.1 (0.9)	5.5 (1.6)

Table 8. The concentrations of propofol in maternal venous blood (MV), in umbilical venous (UV) and arterial (UA) blood after an induction dose of 2.5 mg/kg.

Patient	Time (minutes)	MV (μg/ml)	UV (μg/ml)	UV/MV ratio	UA (μg/ml)	UA/MV ratio
1	4.03	2.66	2.75	1.03	1.73	0.65
2	4.58	3.09	3.14	1.02	2.51	0.81
3	4.75	3.21	2.15	0.67	2.20	0.69
4	5.67	3.12	2.59	0.83	1.42	0.46
5	5.92	3.01	2.14	0.71	1.75	0.58
6	6.00	2.01	2.20	1.09	1.85	0.92
7	6.25	2.63	2.53	0.96	1.77	0.67
8	6.42	2.76	1.65	0.60	1.84	0.67
9	6.43	2.36	2.14	0.91	1.63	0.69
10	7.42	2.10	1.36	0.65	1.25	0.60
Mean	5.75	2.70	2.26	0.85	1.79	0.67
SD	1.02	0.43	0.52	0.18	0.36	0.12

——*——

——**——

——***——

* p=0.058

** p=0.030

*** p=0.0001 (Student's *t*-test).

The concentration of propofol returning to the placenta in umbilical arterial blood is determined by the drug concentration in umbilical venous blood and fetal drug uptake, although some nonplacental drug transfer is also possible.[19] Our results indicate a significant fetal propofol uptake. Rapid placental transfer has also been reported with thiopentone.[20] Thus these facts could cause some unwanted residual effects on neonates. However, no clinically significant depression of the neonates was indicated by the Apgar scores or the blood gas analyses in either the propofol or the thiopentone group.

In conclusion, propofol was found to be similar to thiopentone in induction characteristics and in the effects on the neonates. Recovery times after anaesthesia were shorter with propofol, and this fact may be advantageous in some situations. Propofol appears to be a suitable alternative to thiopentone as an induction agent for anaesthesia in elective Caesarean section.

References

1. Sellick BA. Cricoid pressure to control regurgitation of stomach contents during induction of anaesthesia. *Lancet* 1961; **2:** 404–6.
2. Bland BAR, Lawes, EG, Duncan PW, Warnell J, Downing JW. Comparison of midazolam and thiopental for rapid sequence anesthetic induction for elective ceserean section. *Anesthesia and Analgesia* 1987; **66:** 1165–8.
3. Dundee JW. Intravenous anaesthesia and the need for new agents. *Postgraduate Medical Journal* 1985; **61** (Suppl. 3): 3–6.
4. Ledingham I MCA, Watt I. Influence of sedation on mortality in critically ill multiple trauma patients. *Lancet* 1983; **i:** 1270.
5. Sear JW, Allen MC, Gales M, McQuay HJ, Kay NH, McKenzie PJ, Moore RA. Suppression by etomidate of normal cortisol response to anaesthesia and surgery. *Lancet* 1983; **ii:** 1028.
6. Reddy BK, Pizer B, Bull PT. Neonatal serum cortisol suppression by etomidate compared with thiopentone, for elective caesarean section. *European Journal of Anaesthesiology* 1988; **5:** 171–6.

7. Smith J, Misiak H. Critical flicker frequency (CFF) and psychotropic drugs in normal human subjects—a review. *Psychopharmacology* 1976; **47:** 175–82.
8. Hannington-Kiff JG. Measurement of recovery from outpatient general anaesthesia with simple ocular test. *British Medical Journal* 1970; **3:** 132–5.
9. Maxwell C. Sensitivity and accuracy of the visual analogue scale: a psycho-physical classroom experiment. *British Journal of Clinical Pharmacology* 1978; **6:** 15–24.
10. Cockshott ID, Briggs LP, Douglas EJ, White M. Pharmacokinetcs of propofol in female patients. Studies using single bolus injections. *British Journal of Anaesthesia* 1987; **59:** 1103–10.
11. Winer BJ. *Statistical principles in experimental design*, 2nd edn. New York: McGraw Hill, 1971: 523–46.
12. Stark RD, Binks SM, Dutka VN, O'Connor KM, Arnstein MJA, Glen JB. A review of safety and tolerance of propofol (Diprivan). *Postgraduate Medical Journal* 1985; **61** (Suppl. 3): 152–6.
13. Brooker J, Hull CJ, Stafford M. Effect of lignocaine on pain caused by propofol injection. *Anaesthesia* 1985; **40:** 91–2.
14. Redfern N. Stafford MA, Hull CJ. Incremental propofol for short procedures. *British Journal of Anaesthesia* 1985; **57:** 1178–82.
15. Valtonen M, Iisalo E, Kanto J, Rosenberg P. Propofol as an induction agent in children: pain on injection and pharmacokinetcs. *Acta Anaesthesiologica Scandinavica* 1989; **33:** 152–5.
16. Manner T, Kanto J, Salonen M. Use of simple tests to determine the residual effects of the analgesic component of balanced anaesthesia. *British Journal of Anaesthesia* 1987; **59:** 978–82.
17. Valtonen M, Kanto J, Klossner J. Anaesthesia for cardioversion: a comparision of propofol and thiopentone. *Canadian Journal of Anaesthesia* 1988; **35:** 479–83.
18. Bonati M, Kanto J, Tognoni G. Clinical pharmacokinetics of cerebrospinal fluid. *Clinical Pharmacokinetics* 1982; **7:** 312–35.
19. Kanto J. Obstetric analgesia. Clinical pharmacokinetic considerations. *Clinical Pharmacokinetics* 1986; **11:** 283–98.
20. Kosaka Y, Takahashi T, Mark LC. Intravenous thiobarbiturate anesthesia for cesarean section. *Anesthesiology* 1969; **31:** 489–506.

Anaesthesia, 1989, Volume 44, pages 763–764

Isoflurane inhibits enflurane metabolism in man

M. P. OIKKONEN

Summary

Halogenated inhalation anaesthetics interfere with each other's hepatic microsomal metabolism. The increase in plasma inorganic fluoride concentration, caused by the metabolism of a standardised dose of enflurane, was attenuated by isoflurane given either before or after the enflurane exposure. It is conluded that isoflurane inhibits the metabolism of enflurane in man, a fact that might be advantageous in certain clinical situations.

Key words

Anaesthetics, volatile; enflurane, isoflurane.
Biotransformation; fluorometabolites.

Enflurane anaesthesia occasionally involves the risk of nephrotoxicity induced by inorganic fluoride.[1,2] Halothane inhibits the hepatic microsomal metabolism of enflurane in humans and rats,[3] and isoflurane interferes with the metabolism of halothane in rats.[4] This study was carried out to determine whether isoflurane inhibits the metabolism of enflurane in man, assuming that it would be more sensible to replace enflurane with isoflurane than with halothane, in those cases where an unexpectedly prolonged enflurane exposure might endanger renal function.

Materials and methods

Thirty-three ASA group 1–2 patients scheduled for otorhinolaryngologic surgery were studied (Table 1) after approval by the Ethics Committee of the hospital and informed consent. They had neither hepatic nor renal disease nor took any regular medication known to influence hepatic metabolism. The patients were randomised to three groups to receive isoflurane and enflurane, or enflurane only during two consecutive 60-minute periods, as shown in Table 1. Group E were given enflurane during the first period and thereafter their anaesthetics were continued with nitrous oxide and intravenous drugs. Group EI were first anaesthetised with enflurane and then with isoflurane; in Group IE the order of the two inhalation anaesthetics was reversed.

Premedication was with pethidine and atropine; anaesthesia was induced with thiopentone and fentanyl; suxamethonium was used to facilitate tracheal intubation, and alcuronium and fentanyl were administered as needed in the course of surgery (Table 1). Droperidol 1.25 mg was given at the transition from the first to second period, and Group E received thiopentone (0–125 mg), if necessary during the second period. The anaesthetics were usually continued with the method in use during the second period after the two study periods. Hydration consisted of Ringer's acetate-gluconate at a rate of 5 ml/kg during the first hour of anaesthesia, and 3 ml/kg/hour thereafter.

Ventilation with a Servo ventilator, with 70% nitrous oxide–oxygen was monitored by capnometry. Enflurane (Efrane, Abbott, Italy) and isoflurane (Forane, Abbott, UK) were administered at an inspiratory volume percent appropriate to reach the desired end-tidal concentration (enflurane 0.5%, isoflurane 0.45%) in about 5 minutes and to maintain it stable throughout the period. The end-tidal concentration was measured using a Miran infrared spectrometer (Foxboro Analytical, USA).

The extent of anaesthetic metabolism was assessed by analysis of increases in the concentration of inorganic fluoride in plasma (PF). A sample of venous blood was drawn before inhalation anaesthesia (PF-O), at the end of the first 60-minute period (PF-60), and at the end of the second 60-minute period (PF-120). PF was determined in duplicate using an Orion model 407A Ionalyser, equipped

---

M.P. Oikkonen, MD, Department of Anaesthesia, Otolaryngological Hospital, Helsinki University Central Hospital, Haartmaninkatu 4E, 00290 Helsinki, Finland.

Correspondence should be addressed to Dr M.P. Oikkonen, Department of Anaesthesia, Tampere University Central Hospital, 33520 Tampere, SF-Finland.

Accepted 30 January 1989.

0003–2409/89/090763+02 $03.00/0

© 1989 The Association of Anaesthetists of Gt Britain and Ireland

Table 1. Demographic and anaesthetic data (mean, SD) of three study groups who received isoflurane an enflurane (EI, IE), or enflurane only (E) during two consecutive 60-minute periods.

	Group E Enflurane (n=11)	Group EI Enflurane then isoflurane (n=11)	Group IE Isoflurane then enflurane (n=11)
Sex F/M	3/8	4/7	4/7
Age, years (SD)	39.4 (8.0)	43.8 (8.9)	40.7 (8.3)
Weight, kg (SD)	74.6 (9.6)	70.5 (10.6)	73.1 (11.5)
First 60-minute period	E	E	I
Second 60-minute period	—	I	E
Thiopentone, mg (SD)	390 (96)	289 (59)	307 (64)
Fentanyl, μg (SD)	352 (100)	230 (56)	243 (74)
Alcuronium, mg (SD)	25 (5)	21 (5)	24 (5)

Table 2. The concentration of inorganic fluoride in plasma (PF, μmol/litre) (mean, SD) determined three times (see Materials and methods) during the study.

	Group E Enflurane	Group EI Enflurane then isoflurane	Group IE Isoflurane then enflurane
PF-0	0.6 (0.2)	0.5 (0.2)	0.9 (0.3)
PF-60	7.5 (1.9)	7.3 (1.8)	1.0 (0.2)
PF-120	7.6 (2.2)	5.1 (1.1)	5.5 (1.3)
		†‡	*

$^*<0.05$, when PF-120-IE is compared to PF-60-E or to PF-60-EI;
$^\dagger<0.05$, when PF-120-EI is compared to PF-120-E;
$^\ddagger<0.01$, when PF-120-EI is compared to PF-60-EI (repeated Anova).

with a fluoride-specific electrode (94-09)[5] and the results are presented in μmol/litre (mean, SD). Analysis of variance was used to compare the results; $p < 0.05$ was considered statistically significant.

Results

The concentrations of inorganic fluoride in plasma in the three groups are presented in Table 2 and Figure 1. The 60-minute isoflurane exposure (Group IE) caused no change in PF. PF-60 was equal in groups E and EI (60-minute enflurane exposure), but in comparison, PF-120 was significantly lower in group IE (enflurane preceded by isoflurane). PF-120 was significantly higher in Group E than in Group EI. The decrease in PF was statistically significant in Group EI during the second 60-minute isoflurane exposure, whereas no decrease was found in Group E during the hour after the enflurane administration.

Discussion

Halogenated inhalation anaesthetics are believed to be metabolised by substrates of various subtypes of enzymes belonging to the hepatic mixed function oxidase system.[6] The inhibition of enflurane metabolism by halothane[3] might indicate overlapping in binding of the volatile anaesthetics to microsomal enzymes.

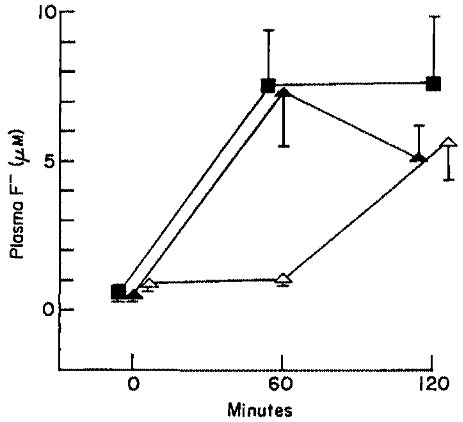


Fig. 1. The mean (SD) concentrations of inorganic fluoride in plasma in the three groups of patients studied: ■, enflurane then intravenous medication and nitrous oxide; ▲, enflurane then isoflurane; △, isoflurane then enflurane.

Isoflurane, being an isomer of enflurane, should theoretically compete with enflurane for binding sites. However, the inhibition of oxidative and slight enhancement of reductive halothane metabolism by isoflurane is proposed to result from the interference of isoflurane with the oxygen-generating system, and not from competition.[4] If this assumption is true, liberation of inorganic fluoride, linked to oxidative enflurane metabolism, should be decreased by isoflurane, which agrees with the results of this study.

Whatever the molecular mechanism, isoflurane slows down enflurane metabolism that liberates inorganic fluoride in man. This fact might be of interest for anaesthetists worried by the risk of inorganic fluoride-induced nephrotoxicity, in cases when enflurane exposures unexpectedly become prolonged. Then, the substitution of enflurane with isoflurane might present certain advantages: tissue depots of enflurane are exhaled with the result that recovery from anaesthesia is rapid and there is reduced liberation of inorganic fluoride. The risk of nephrotoxicity should also be counteracted because of inhibition by isoflurane of the metabolism of enflurane. However, the quantitative profit of the isoflurane–enflurane interaction remains to be documented in connexion with long enflurane exposures.

References

1. Eichhorn JH, Hedley-Whyte J, Steinman TI, Kaufmann JM, Laasberg LH. Renal failure following enflurane anesthesia. *Anesthesiology* 1976; **45:** 557–60.
2. Mazze RI, Calverley RK, Smith NT. Inorganic fluoride nephrotoxicity. Prolonged enflurane and halothane anesthesia in volunteers. *Anesthesiology* 1977; **46:** 265–71.
3. Fish KJ, Rice SA. Halothane inhibits metabolism of enflurane in Fischer 344 rats. *Anesthesiology* 1983; **59:** 417–20.
4. Fiserova-Bergerova V. Inhibitory effect of isoflurane upon oxidative metabolism of halothane. *Anesthesia and Analgesia* 1984; **63:** 399–404.
5. Fry BW, Taves DR. Serum fluoride analysis with the fluoride electrode. *Journal of Laboratory and Clinical Medicine* 1970; **75:** 1020–5.
6. Ivanetich KM, Lucas SA, Marsh JA. Enflurane and methoxyflurane. Their interaction with hepatic cytochrome P-450 *in vitro*. *Biochemical Pharmacology* 1979; **28:** 785–92.

Anaesthesia, 1989, Volume 44, pages 765–766

CASE REPORT

An unusual case of symptomatic hypoglycaemia in a child

T. M. W. LONG

Summary

An unusual case of pre-operative, symptomatic hypoglycaemia in an otherwise fit, well developed 6-year-old boy is reported, and highlights the unpredictable effect of pre-operative starvation on children admitted on the day of surgery. The presentation and incidence of hypoglycaemia before operation in children is also reviewed.

Key words

Anaesthesia: paediatric.
Metabolism: hypoglycaemia.

Hypoglycaemia after pre-operative starvation is described in small and underweight infants, but is more unusual in older children. The usual instructions in daycase surgery are for the child to arrive fasted from food and drink from the night before the operation. This case report describes a child who developed symptomatic hypoglycaemia on this regimen.

Case history

A 6-year-old negroid boy (Sickle-cell negative) was admitted for adenotonsillectomy on the morning of surgery. He was seen before operation by the author at 0830 hours. He weighed 32 kg, and apart from chronic symptoms that related to his enlarged adenoids and inflamed tonsils, he was generally fit, well, alert and communicative.

He had had a daycase general anaesthetic when 2 years 3 months old, for cautery to the nose to treat repeated epistaxes. The anaesthetic and recovery were unremarkable. He had no other significant previous medical history. His mother, as instructed, had ensured that he had had nothing by mouth from midnight the night before. No premedication was prescribed.

The boy was brought to the anaesthetic room at 1045 hours. He was found to be drowsy, confused, cold, clammy and sweaty. He complained incoherently of severe upper abdominal pain which caused him to lie curled up on the trolley. His mucosal surfaces were pink and well perfused, sublingual temperature 35.5°C and pulse rate 90 beats/minute, with good volume. His abdomen was soft, but generally tender over the epigastrium; bowels sounds were present as normal. It was not until, as part of his incoherent ramblings, he repeatedly complained of great hunger, that the clinical diagnosis of hypoglycaemia was made.

Immediately a BM stick (Boehringer Mannheim BM test Glyceime 1-44) estimation of his blood glucose was performed, which showed a level of 2.0 mmol/litre. A peripheral vein on his left hand was then cannulated and a sample of blood taken for laboratory measurement of blood glucose. This later revealed a blood glucose of 3.2 mmol/litre using an Analox Glucostat analyser, which has an accuracy of SD 0.1 mmol/litre.

Surgery was abandoned and quick treatment with 50% dextrose 25 ml intravenously produced a rapid improvement in his condition. Treatment was continued with a 5% dextrose infusion at 70 ml/hour. He was then sent back to the ward for a milk drink and food. He continued to make a full recovery and was back to normal by lunchtime. Blood glucose at that time was 6.2 mmol/litre by laboratory measurement.

Discussion

The unusual features of this case are that an otherwise fit, healthy, stocky child should develop such florid symptoms and signs of hypoglycaemia before operation after a long period of starvation. The normal range of fasting blood glucose at our laboratory is 3.3–5.6 mmol/litre and this is in keeping with other quoted values for adults. However, there is disagreement about the lower limit of normal in children, and quoted values range from 3.3 mmol/litre[2], to 2.8 mmol/litre[3] and 2.2 mmol/litre.[4,5]

T.M.W. Long, BM, BS, FFARCS, Senior Registrar, Anaesthetic Department, Queen Elizabeth Hospital, Edgbaston, Birmingham.

Accepted 31 January 1989.

0003–2409/89/090765+02 $03.00/0 © 1989 The Association of Anaesthetists of Gt Britain and Ireland

Thus, our patient had a pre-operative blood glucose only marginally below the highest accepted lower limit for a fasting blood glucose, but had marked symptoms and signs of hypoglycaemia. This would not normally be expected until the blood glucose was below 2.2 mmol/litre.[6] Furthermore, in many studies children with blood glucoses below 3.3 mmol/litre showed no signs of hypoglycaemia,[2,4,7–9] and even those children with a blood glucose below 2.2 mmol/litre were asymptomatic.[2,10]

This boy was particularly sensitive to the lowering of his blood glucose, although detailed questioning of his mother revealed that he was a normal, healthy, active child with appetite and eating habits appropriate for his age and size. He had had a previous general anaesthetic at the age of 2 years 3 months when he weighed 15 kg, and had coped with the pre-operative starvation on that day. Workers have suggested that hypoglycaemia after pre-operative starvation is more likely in children less than 4 years old and less than 15 kg weight,[9] or those children whose weight is below the third centile for their age.[11] But the boy in this case was 6 years old and weighed 32 kg, and so was above the 90th centile for his age.

The instructions to parents of children admitted on the day of surgery at this hospital are: 'the child should have nothing to eat or drink from midnight of the day before operation', which is an accepted policy.[8] This boy, had his tea at 1730 on the evening before surgery and a drink of milk before going to bed at 1930 and nothing afterwards. Therefore, he was starved for a total 15 hours 15 minutes before being brought to the anaesthetic room. Children generally tolerate prolonged periods of starvation,[8] even up to 24 hours, despite nearly 25% of them having blood glucose levels below 2.2 mmol/litre.[10] The reported incidence of biochemically confirmed hypoglycaemia (< 3.3 mmol/litre) is between 0 and 15% in children pre-operatively starved,[2,4,7–9,11] but none of those studies reported any signs or symptoms of hypoglycaemia.

A full medical review of this boy has not revealed any underlying syndrome or disease process to explain his response to the starvation, so he must be considered to have an exaggerated response to slightly lowered blood glucose. Hypoglycaemia is rare but one must be aware of it and treat it without delay to avoid permanent central nervous system damage.

References

1. THE MEDICINE PUBLISHING FOUNDATION. *Normal values in medicine*, 3rd edn. Oxford: The Medicine Group, 1987.
2. ALLISON CW, CATER JI, GRAY IG, STAZIKER AC. Pre-operative starvation in children. *Anaesthesia* 1982; **37:** 274–7.
3. EHRLICH RM. Hypoglycaemia in infancy and childhood. *Archives of Disease in Childhood* 1971; **46:** 716–9.
4. WATSON BG. Blood glucose levels in children during surgery. *British Journal of Anaesthesia* 1972; **44:** 712–5.
5. HABBICK BF, MCNEISH AS, STEPHENSON JBP. Diagnosis of ketotic hypoglycaemia of childhood. *Archives of Disease in Childhood* 1971; **46:** 295–300.
6. PAGLIARA AS, KARL IE, HAYMOND M, KIPNIS DM. Hypoglycemia in infancy and childhood. Part 1. *Journal of Paediatrics* 1973; **82:** 365–79.
7. SCHNEIDER BM, NAHRWOLD ML. Fasting plasma glucose in children. *Anesthesiology* 1982; **57** (Suppl.): A430.
8. JENSEN BH, WERNBERG M, ANDERSEN M. Pre-operative starvation and blood glucose concentrations in children undergoing inpatient and outpatient anaesthesia. *British Journal of Anaesthesia* 1982; **54:** 1071–74.
9. THOMAS DKM. Hypoglycaemia in children before operation: its incidence and prevention. *British Journal of Anaesthesia* 1974; **46:** 66–8.
10. CHAUSSAIN JL. Glycemic response to 24-hour fast in normal children and children with ketotic hypoglycemia. *Journal of Pediatrics* 1973; **82:** 438–43.
11. PAYNE K, IRELAND P. Plasma glucose levels in the perioperative period in children. *Anaesthesia* 1984; **39:** 868–72.

Anaesthesia, 1989, Volume 44, pages 767–769

CASE REPORT

Anaphylactoid reaction to chymopapain

M. B. SMITH AND V. C. HOFMANN

Summary

Chymopapain is a proteolytic enzyme used in the chemonucleolysis of the herniated nucleus pulposus of lumbar intervertebral discs. It causes rapid hydrolysis of the noncollagenous polypeptides that maintain the tertiary structure of the chondromucoprotein of the nucleus pulposus. We report here an anaphylactoid reaction after the intervertebral injection of chymopapain.

Key words

Allergy.
Pharmacology; chymopapain.

Chymopapain is used in the treatment of herniated nuclei pulposii of the lumbar intervertebral discs which cause symptoms that have not resolved with more conservative management. Over 160 000 cases have been so treated worldwide. Its use is complicated by both neurotoxic effects and the risk of anaphylactoid reactions. We report here a delayed, severe anaphylactoid reaction to the injection of chymopapain.

Case history

A 29-year-old, ASA 1, 80-kg male patient presented for surgery with a 12-month history of lower back pain which radiated to his posterior left thigh and calf. Conservative management had failed to improve his condition. A lumbar myelogram showed an extradural defect at the level of L_{4-5}, with the typical appearance of a herniated nucleus pulposus. It was decided to proceed with a radiographically controlled intervertebral injection of chymopapain under general anaesthesia.

Pre-operative anaesthetic assessment revealed two previous uncomplicated general anaesthetics. The patient had no other past medical history, no known allergies or family history thereof. He smoked two packets of cigarettes a day and consumed significant quantities of alcohol. A physical examination found no abnormalities. Chest X ray, electrocardiogram and haematological investigations were all within normal limits. He had been taking cimetidine and diphenhydramine every 6 hours for the previous 24 hours as pretreatment of the histamine receptors.

The patient gave informed consent for general anaesthesia and was premedicated with diazepam and cimetidine on the morning of surgery. An intravenous cannula was placed in a peripheral vein and an infusion of 5% dextrose and lactated Ringer's solution started.

He was positioned supine on the operating table. Baseline arterial blood pressure was 110/70 mmHg and pulse rate 80 beats/minute. Anaesthesia was induced with thiopentone after pre-oxygenation and defasciculation with tubocurare. Neuromuscular blockade was achieved with suxamethonium and the patient's trachea intubated. Anaesthesia was maintained with fentanyl, isoflurane and pancuronium and he was turned to the right lateral decubitus position. The arterial blood pressure was 100/60 mmHg and the pulse rate 90 beats/minute. Diphenhydramine 50 mg was given intravenously before surgery started.

A 22-gauge needle was placed into the centre of the L_{4-5} disc space. A discogram was obtained using metrizamide-60, and the position of the needle tip verified with antero-posterior and lateral fluoroscopy. Chymopapain 3000 units in 1.5 ml were injected and after 3 minutes the patient was repositioned supine.

Heart sounds heard through the oesophageal stethoscope were now noticed to be reduced, heart rate had increased rapidly and blood pressure was unrecordable. The patient's colour began to deteriorate and cardiopulmonary resuscitation was started. Ventilation was continued with 100% oxygen, and diphenhydramine 50 mg, dexamethasone 4 mg, adrenaline 1 mg and 100 ml 8.4% sodium bicarbonate were given. Cardiac compression produced a faint carotid pulse.

M.B. Smith, FFARCS, Visiting Assistant Professor, V.C. Hofmann, FFARCS, Associate Professor, Department of Anesthesiology, University of Oklahoma, Health Science Center, Post Office Box 26901, Oklahoma City, Oklahoma 73190, USA.

Accepted 3 February 1989.

0003–2409/89/090767+03 $03.00/0

© 1989 The Association of Anaesthetists of Gt Britain and Ireland

The drugs were repeated: 1 mg adrenaline, 100 mg hydrocortisone, 100 ml 8.4% sodium bicarbonate, 500 μg phenylephrine, 50 mg ephedrine and 500 mg calcium chloride, but there was still no cardiovascular response. A second intravenous line was secured and 4 litres of lactated Ringer's solution were given. Arterial blood gases showed pH 7.34, $Pa\text{CO}_2$ 7.1 kPa, $Pa\text{O}_2$ 17.3 kPa. A faint carotid pulse was now palpable and the ECG showed a sinus tachycardia, but the blood pressure was still unrecordable. Further drug therapy consisted of 1 mg adrenaline, 50 ml 8.4% sodium bicarbonate, 50 mg ephedrine, 500 μg phenylephrine and 100 mg hydrocortisone. The blood pressure now measured 70 mmHg systolic and chest compressions were stopped. Arterial blood gases were repeated and showed pH 7.28, $P\text{CO}_2$ 6.9 kPa, $P\text{O}_2$ 9.9 kPa. Minute ventilation was increased and 50 ml 8.4% sodium bicarbonate was given together with hydrocortisone 100 mg. The patient's blood pressure was 120/80 mmHg and pulse rate 120 beats/minute after 45 minutes of resuscitation.

An arterial and a central venous pressure line were now inserted. The patient was transfered to the intensive care unit where artificial ventilation was continued, after stabilisation of physiological variables. His trachea was extubated on the third postoperative day, when he was awake with stable respiratory and cardiovascular systems. His left upper extremity was oedematous and slightly cool, but brachial, radial and ulnar pulses were detected with the Doppler. His recovery continued over the following days. The swelling of the left arm decreased, perfusion increased and he was discharged on the 7th postoperative day.

Discussion

Chemonucleolysis is the term used to describe the injection of a proteolytic enzyme into the intervertebral space to hydrolyse the chondromucoprotein complex that causes pressure on nerve roots.[1] Chymopapain was approved by the Federal Drug Administration of America in 1982 for intradiscal injection to treat patients with documented herniated lumbar intervertebral discs, when signs and symptoms had not responded to conservative therapy.[2] Chymopapain was isolated and purified from the leaf of the tropical papaya plant in 1941[3] and first used for the treatment of prolapsed intervertebral discs in 1959.[4] A multicentre, controlled, double-blind trial in 1981[5] demonstrated chymopapain as effective in 91% of patients for the treatment of herniated lumbar discs, and this led directly to the recognition of the drug for clinical use.

Chymopapain, once injected into the intervertebral space, causes rapid hydrolysis of the noncollagenous polypeptides that maintain the tertiary structure of the chondromucoprotein of the nucleus pulposus. Degradation of the chondromucoproteins reduces intradiscal osmotic activity, decreases fluid absorption and lessens intradiscal pressure.[6,7] There is a transient increase in urinary mucopolysaccharides after injection.[8] The enzymatic activity of chymopapain is inhibited by a natural proteolytic enzyme inhibitor, alpha$_2$-macroglobin, in plasma. There is no proteolytic activity by chymopapain expressed outside the disc.[9] The most recent formulation of chymopapain contains two enzymatically active components and cysteine as a reducing agent. It does not contain sodium bisulphate.[8]

Serious neurological adverse events, within hours or days, occur in about 1:2000 patients injected with chymopapain. Needle trauma or chymopapain injection with contrast media into spinal fluid may account for some of these adverse events. Acute transverse myelitis or myelopathy has been reported in association with chymopapain injection, at the rate of 1 in 18 000. These patients are characterised clinically by a delay of 2–3 weeks before the onset of symptoms of paraplegia or paraparesis.[8] Discography was performed as part of the procedure in nearly all the severe neurological adverse events.[1] Certain contrast media are known to be neurotoxic when injected intrathecally.[10] Their toxicity is enhanced by bleeding. Chymopapain intrathecally causes disruption of capillaries and may cause bleeding.[7] Nearly all the patients who experienced serious neurological sequelae had the injection of chymopapain performed under general anaesthesia.[1] When performed under local anaesthesia an awake patient will experience pain when the needle impinges on nerve tissue.[8]

The most serious adverse reaction to the injection of chymopapain is anaphylactic in nature. The incidence of such reactions is approximately 1%, and several deaths have been reported.[1] The anaphylaxis rate is statistically significantly higher in females (0.9% versus 0.3% for males) and for patients who receive general anaesthesia (0.6% versus 0.4% for local anesthesia).[8] The overall mortality rate after chymopapain injection is approximately 1 in 5000 patients (0.02%).[11] The mortality rate associated with laminectomy has been reported in the range of 0.02% to 0.1%.[8]

Skin tests and specific IgE immunoassay are recommended in patients who present for chemonucleolysis and give a history of previous exposure to chymopapain and chymopapain-like material. Papaya or its derivatives are found in meat tenderisers, papaya protein, carotenoid products, beer brewed in the United States and contact lens cleaning fluid.[12] Previous treatment with chymopapain increases the risk of anaphylaxis.

Pre-operative administration of drugs to decrease the incidence or severity of an intra-operative reaction in general, and chymopapain anaphylaxis in particular, has been recommended.[13,14] This would include H_1 and H_2 receptor antagonists and corticosteroids. The patient in this case was premedicated with cimetidine and diphenhydramine for 24 hours. Receptor binding data for diphenhydramine show that a maximum of 20% of the receptors can be bound.[15] There is no reported series in which premedication has reduced the anaphylaxis rate, but data with contrast media reactions have demonstrated the efficacy of premedication in decreasing the incidence and severity of allergic reactions.[10]

All fluids given in sufficient amounts will restore the intravascular circulating volume. The major risk associated with fluid resuscitation is the development of pulmonary oedema. The effects of colloid and crystalloid solutions on pulmonary function have been extensively studied. It is claimed that resuscitation with colloids produces less pulmonary dysfunction,[16,17] in part by maintenance of the colloid oncotic pressure.[18,19] However, it has been shown that colloids and crystalloids have equivalent effects on pulmonary function and extravascular lung water,[20] even if the pulmonary capillary permeability is increased with oleic acid.[21] Crystalloids have the advantage of rapid availability, no antigenicity, no infectious disease to transmit, no interference with coagulability and are inexpensive. The possibility in this case of pulmonary oedema was further reduced by postoperative positive pressure ventilation.

The intra-operative management of an anaphylactoid reaction and volume resuscitation with crystalloid is well demonstrated with this case. There was a delay in onset of signs of anaphylaxis of approximately 3 minutes after the injection of chymopapain.

References

1. Manchikanti L, Meriwether RP, Grow JB. Anesthetic management of patients for chemonucleolysis. *Anesthesiology Review* 1985; **10:** 35–45.
2. Willis J. Chymopapain approved. *Federal Drug Administration Drug Bulletin* 1982; **12:** 17–8.
3. Jansen EF, Balls AK. Chymopapain. A new crystalline protease from papaya-latex. *Journal of Biology and Chemistry* 1941; **137:** 459–63.
4. Smith L. Enzyme dissolution of the nucleus pulposus in humans. *Journal of the American Medical Association* 1964; **187:** 137–40.
5. Javid MJ, Nordby EJ, Ford LT, Hejna WJ, Whisler WW, Burton C, Millett DK, Wiltse LL, Widell EH, Boyd RJ, Newton STE, Thisted R. Safety and efficacy of chymopapain T (Chymodiactin) in herniated nucleus pulposus with sciatica. Results of a randomized, double-blind study. *Journal of the American Medical Association* 1983; **249:** 2489–94.
6. Stern IJ, Smith L. Dissolution by chymopapain *in vitro* of tissue from normal or prolapsed intervertebral discs. *Clinical Orthopaedics and Related Research* 1967; **50:** 269–77.
7. Garvin PJ, Jennings RB, Smith L, Gesler RM. Chymopapain: a pharmocologic and toxicologic evaluation in experimental animals. *Clinical Orthopaedics and Related Research* 1965; **42:** 204–23.
8. Smith Laboratories. Product Information, Chymodiactin (chymopapain). 2215 Sanders Road, Northbrook, IL 60062, USA.
9. Kapsalis AA, Stern IJ, Bornstein I. Correlation between hypersensitivity to parenteral chymopapain and the presence of IgE anti-chymopapain antibody. *Clinical and Experimental Immunology* 1978; **33:** 150–8.
10. Goldberg M. Systemic reactions to intravascular contrast media. A guide for the anesthesiologists. *Anesthesiology* 1984; **60:** 46–56.
11. Gundy P. What is intradiscal therapy anyway? *Journal of the American Medical Association* 1983; **249:** 1120–3.
12. Bernstein DI, Gallagher JS. Local ocular anaphylaxis to papain enzyme contained in contact lens cleaning solution. *Journal of Allergy and Clinical Immunology* 1984; **74:** 258–60.
13. Beaven MA. Anaphylactoid reactions to anesthetic drugs. *Anesthesiology* 1981; **55:** 3–5.
14. Millbern SM, Bell SD. Prevention of anaphylaxis to contrast media. *Anesthesiology* 1979; **50:** 56–7.
15. Moss J, Fahmy NR, Sunder W, Beaven MA. Hormonal and hemodynamic profile of an anaphylactic reaction in man. *Circulation* 1981; **63:** 210–3.
16. Rackow EC, Falk JL, Fein IA, Seigal JS, Packman MI, Haupt MT, Kaufman BS, Putman D. Fluid resuscitation in circulatory shock: A comparison of the cardiorespiratory effects of albumin, hetastarch and saline solutions in patients with hypovolaemic and septic shock. *Critical Care Medicine* 1983; **11:** 839–50.
17. Shoemaker WC, Hauser CJ. Critique of crystalloid versus colloid therapy in shock and shock lung. *Critical Care Medicine* 1979; **7:** 117–24.
18. Weil MH, Henning RJ, Puri VK. Colloid oncotic pressure: Clinical significance. *Critical Care Medicine* 1979; **7:** 113–6.
19. Rackow EC, Fein IA, Seigal J. The relationship of the colloid osmotic-pulmonary artery wedge pressure gradient to pulmonary oedoma and mortality in critically ill patients. *Chest* 1982; **82:** 433–7.
20. Gallagher J, Banner MJ, Barnes PA. Large volume crystalloid resuscitation does not increase extravascular lung water. *Anesthesia and Analgesia* 1985; **64:** 323–6.
21. Pearl RG, Halperin BD, Mihm FG, Rosenthal MH. Pulmonary effects of crystalloid and colloid resuscitation from haemorrhagic shock in the presence of oleic acid induced pulmonary capillary injury in the dog. *Anesthesiology* 1989; **68:** 12–20.

Anaesthesia, 1989, Volume 44, pages 770–772

CASE REPORT

Peripartum cardiomyopathy

A rare cause of pulmonary oedema in late pregnancy

N. G. LAVIES AND D. A. B. TURNER

Summary

A case of peripartum cardiomyopathy that occurred together with pre-eclampsia is described. This gave rise to pulmonary oedema at 36 weeks' gestation. Intensive care management and the need for invasive monitoring, especially pulmonary artery wedge pressure, of patients who develop pulmonary oedema in the peripartum period is discussed.

Key words

Complications; peripartum cardiomyopathy.

Cardiomyopathy of pregnancy, or peripartum cardiomyopathy, is a rare condition which presents clinically with the onset of cardiac failure in the last month of pregnancy, or the first 5 postpartum months. There should be no obvious aetiology for the cardiac failure and no evidence of demonstrable heart disease before the last month of pregnancy.[1-3] The diagnosis becomes confused and therapeutic efforts may be misdirected when pre-eclampsia occurs together with peripartum cardiomyopathy. We describe such a patient who required intensive care management.

Case history

A 23-year-old Caucasian primigravida was admitted to a District General Hospital at 36 weeks' gestation because of marked peripheral oedema and proteinuria of 3 g/24 hours. She was known to have a fetus with an abdominal wall defect, and for this reason was booked into the regional paediatric referral centre for delivery. Her arterial blood pressure did not increase initially, but she was noted to be anaemic.

She complained of tightness in her chest the day after admission. Her blood pressure was 150/85 mmHg and heart rate 130 beats/minute on examination, but her chest was clear on auscultation. That night her membranes ruptured spontaneously, so she was transferred to the regional centre with an infusion of ritodrine as a tocolytic agent.

On arrival, her arterial pressure was 140/95 mmHg; she had 2+ proteinuria, and a diagnosis of mild to moderate pre-eclampsia was made. A lumbar epidural catheter was inserted and 0.25% bupivacaine 8 ml administered. She also received approximately 1500 ml crystalloid intravenously. She complained of shortness of breath and chest pain one hour later. On examination, her arterial blood pressure was 160/110 mmHg, heart rate 140 beats/minute and bilateral basal crepitations were present. A chest X ray confirmed pulmonary oedema and she was given frusemide intravenously.

A decision to perform urgent Caesarean section was then made. A central venous line was inserted via an antecubital vein and its position confirmed on X ray. This gave an initial reading of zero (referred to right atrium). Caesarean section was performed under general anaesthesia and a live male infant who weighed 3180 g, with the expected gastroschisis, was delivered. There were no intra-operative problems and on recovery her blood pressure was 150/110 mmHg, central venous pressure (CVP) 4 cm H_2O, heart rate 110 beats/minute and respiratory rate 32 breaths/minute. A good diuresis occurred in response to frusemide and this was followed by clinical improvement. However, the basal crepitations persisted.

She suffered an exacerbation of her pulmonary oedema during the night; she became acutely breathless, her CVP rose to 7 cm H_2O and heart rate to 175 beats/minute. This episode responded to further frusemide and diamorphine. The next 48 hours saw very little overall improvement. She remained clinically and radiologically in pulmonary oedema with a persistent sinus tachycardia of 130–140 beats/minute. An ECG performed 2 days postpartum showed widespread T-wave inversion in the anterior chest leads.

She was transferred to the Intensive Care Unit at this stage, for further management. A balloon tipped flow-directed pulmonary artery catheter was inserted and the initial pulmonary artery wedge pressure (PAWP) was 30

N.G. Lavies, BSc, MB, ChB, FFARCS, Senior Registrar, D.A.B. Turner, MB, BS, FFARCS, Consultant, Department of Anaesthesia, Leicester Royal Infirmary, Leicester LE1 5WW.

Accepted 6 March 1989.

0003–2409/89/090770+03 $03.00/0

© 1989 The Association of Anaesthetists of Gt Britain and Ireland

mmHg (pulmonary artery pressure 44/35 mmHg). An echocardiogram showed a dilated left ventricle and a low ejection fraction.

She was therefore treated with an isosorbide infusion, digoxin and diuretics, and improved markedly over the next 3 days and did not require artificial ventilation. She was well enough to be transferred to the regional cardiothoracic unit for detailed assessment after a further 3 days. Echocardiography again revealed a dilated left ventricle with poor cardiac contraction and also demonstrated mitral regurgitation and paradoxical movement of the septum. A diagnosis of peripartum cardiomyopathy was therefore considered. She continued to improve and on the 18th day postpartum she was discharged home after complete radiological resolution of pulmonary oedema and cardiomegaly. Subsequent follow up shows her to remain well.

Discussion

Pulmonary oedema in the parturient usually occurs postpartum and in association with severe pre-eclampsia. The underlying mechanism in this situation appears to be a pulmonary capillary membrane leak and (or) low colloid osmotic pressure, often precipitated by intravenous fluid therapy and postpartum fluid shifts.[4] Less commonly, pulmonary oedema in the pre-eclamptic develops antepartum and is then more likely to be because of left ventricular failure.[4,5] However, it is unclear in this situation whether the aetiology represents a true cardiomyopathy or is simply hypertensive heart failure as a result of increased afterload.[5]

Cardiac failure can develop in the peripartum period without any evidence of pre-eclampsia, and a diagnosis of cardiomyopathy must then be considered after other causes, such as myocardial infarction, have been excluded. The relationship between peripartum cardiomyopathy and pre-eclampsia is not entirely clear but most authors now believe that pre-eclampsia has no direct aetiological role in the development of the cardiomyopathy,[2] although the former occurs in 22% of cases.[1] Confusion can arise when they occur together.[3]

Initially, the pulmonary oedema in our patient, was attributed to a low colloid osmotic pressure and a capillary membrane leak as a result of pre-eclampsia. Her serum albumin was low and she received 1500 ml of crystalloid intravenously in a short space of time. One alternative explanation was the ritodrine infusion given to her during transfer from the district general hospital, since this drug has been implicated in the development of pulmonary oedema in pregnancy.[6,7] However, this is unlikely because she only received ritodrine for a short time, and moreover the dyspnoea and tachycardia developed beforehand. Cardiac failure was not suspected at this stage because the hypertension was not severe and the CVP not increased.

The true cause of her pulmonary oedema, left ventricular dysfunction, only became apparent on the third postpartum day after the insertion of a pulmonary artery catheter which revealed a very high PAWP. She responded rapidly to preload reduction, with radiological resolution over the next 2 weeks. Strauss *et al.*[5] argued that afterload reduction with sodium nitroprusside is more appropriate, but their patients were more severely hypertensive and management was based on the premise of hypertensive heart failure.

We believe that our patient had peripartum cardiomyopathy. She developed prodromal symptoms and signs prior to hypertension and the degree of hypertension was never severe. Later she had the characteristic clinical features of left ventricular dilatation, low ejection fraction, gallop rhythm, functional mitral regurgitation and nonspecific T-wave changes on ECG.[1-3] Significant cardiac enlargement and cardiac arrhythmias are unusual in pre-eclampsia alone.[2]

She had several uncharacteristic features, however; she was young, Caucasian and primigravid, and presented antepartum. There have been occasional reports in similar patients,[8,9] but it is a condition which is either rare or not often recognised in Caucasians. The long-term prognosis of peripartum cardiomyopathy depends on whether the heart size returns to normal quickly; 50% still had cardiomegaly at 6 months in the series of Demakis *et al.*[1] and their prognosis was very poor. Our patient's heart size returned to normal by 2 weeks and we speculate that this favourable outcome was because of appropriate monitoring and intensive therapy, which may not have been available at the time of the previous series.

The place of invasive haemodynamic monitoring, and in particular measurement of PAWP, in pre-eclampsia is not yet firmly established.[10] Even CVP monitoring is not universally accepted by obstetricians in the UK as necessary in severe pre-eclampsia. When is pulmonary artery catheterisation indicated in these patients? Benedetti *et al.*[4] in a report of 10 pre-eclamptics who developed pulmonary oedema, concluded that differences between CVP and PAWP are only likely to be clinically relevant when the CVP is greater than 6 cm H_2O. However, this is not supported by this case report.

This case illustrates that pulmonary oedema in late pregnancy presents a difficult differential diagnosis which includes capillary membrane leak, low colloid osmotic pressure and left ventricular failure, or combinations of these. Rational management requires measurement of the PAWP since this cannot be reliably predicted from the CVP even if the latter is low. We therefore agree with Wasserstrum and Cotton[10] that the development of pulmonary oedema *per se* represents a strong indication for pulmonary artery catheterisation. If the PAWP is normal or low, increased capillary permeability with or without low colloid osmotic pressure can be assumed to be the cause and diuretics are then inappropriate. The appropriate management includes vasodilators and diuretics if the PAWP is high, as in this case.

References

1. Demakis JG, Rahimtoola SH. Peripartum cardiomyopathy. *Circulation* 1971; **44:** 964–8.
2. Julian DG, Szekely P. Peripartum cardiomyopathy. *Progress in Cardiovascular Diseases.* 1985; **27:** 223–40.
3. Homans DC. Current Concepts: Peripartum Cardiomyopathy. *New England Journal of Medicine* 1985; **312:** 1432–7.
4. Benedetti TJ, Kates R, Williams V. Hemodynamic observations in severe preeclampsia complicated by pulmonary edema. *American Journal of Obstetrics and Gynecology* 1985; **152:** 330–4.
5. Strauss RG, Keefer JR, Burke J, Civett JM. Hemodynamic monitoring of cardiogenic pulmonary edema complicating toxemia of pregnancy. *Obstetrics and Gynecology* 1980; **55:** 170–4.
6. Marks RJ, De Chazal RCS. Ritodrine-induced pulmonary oedema in labour. Successful management using epidural anaesthesia. *Anaesthesia* 1984; **39:** 1012–4.

7. Benedetti T, Hargrove J, Rosene KA. Maternal pulmonary edema during premature labor inhibition. *Obstetrics and Gynecology* 1982; **59:** 335–7S.
8. Phipps JH, Rashid J, Griffin DR. Postpartum collapse due to acute dilated cardiomyopathy. *Lancet* 1987; **1:** 1500.
9. Grace AA, Jenkins RE, King MJ. Peripartum cardiomyopathy. *Lancet* 1987; **2:** 575.
10. Wasserstrum N, Cotton DB. Hemodynamic monitoring in severe pregnancy-induced hypertension. *Clinics in Perinatology* 1986; **13:** 781–99.

Anaesthesia, 1989, Volume 44, pages 773–774

CASE REPORT

Obliteration of the axillary artery after axillary block

B. OTT, L. NEUBERGER AND H. P. FREY

Summary

A case of total obliteration of the axillary artery after axillary block is presented. This resulted from an accidental intramural injection of local anaesthetic (mepivacaine 1%, 40 ml, with adrenaline 1:200 000). Axillary block was performed using the loss of resistance technique with a blunt needle (45° bevel). The diagnosis was made by palpation of the peripheral pulse and by comparison between the skin temperatures of each arm. The thrombosed part of the artery was successfully reconstructed with an autologous saphenous vein graft.

Key words

Arteries; axillary, damage.
Anaesthetic techniques; regional, axillary.

Axillary block is frequently used for operations on the arm. Serious complications after this method are relatively rare.[1,2] We present a case in which the use of this technique caused an 8-cm dissection of the axillary artery which resulted in thrombotic obliteration of the lumen of the vessel. There was no acute ischaemia because of abundant collateral vessels in this region. The patient had relatively minor symptoms from the closure of the artery and the diagnosis was made 2 weeks after the operation.

Case history

The patient was a 16-year-old obese (110 kg) man scheduled for an arthrodesis of his right thumb with regional anaesthesia. An intravenous infusion was set up in the left arm and the right upper arm was abducted to 90°. The patient was supine. The axillary region was cleaned and covered with sterile drapes.

Palpation of the axillary artery at the lower side of the pectoral muscle was difficult because of the patient's obesity and its localisation took a somewhat longer time than usual. A 5-cm, blunt, 23-gauge needle was introduced into the sheath around the vascular and nervous structures with the loss-of-resistance technique and placed in front of the artery.[3-5] The arterial pulsations were transmitted to the needle and were felt easily. Arterial puncture was not seen and blood was not aspirated through the needle. There was no haematoma. Paraesthesiae were neither sought nor elicited. Forty millilitres mepivacaine 1% with adrenaline 1:200 000 was injected with intermittent aspiration to exclude an intravascular injection. There were no problems with the injection; no atypical increased resistance and no spasm of the artery.[6] A sympathetic, sensory and motor block was established within minutes.

The postoperative course was without problems and the patient left the hospital on the second day. When the patient came for examination 14 days later he complained about an unusual feeling of cold in the right arm. There was an obvious difference in temperature between the two hands and there was no palpable pulse on the right side. Investigation with ultrasound[7] (Doppler) showed that the axillary artery was probably occluded, and angiography showed a filling defect of the axillary artery just distal to the branch forming the subscapular artery (Fig. 1). Revision and reconstruction of the artery were indicated.

A 5-cm fibrotic and hard segment of the axillary artery was seen at the beginning of the operation. There were normal pulsations above the subscapular artery, and distal to the fibrotic segment the axillary artery was continued in a soft and empty brachial artery. An 8-cm thrombus was removed from the dissected intima after arteriotomy. Simple reconstruction with a 10-cm length of saphenous vein, inserted distal to the subscapular artery, was performed. The postoperative course was uneventful and the patient had normal blood flow and strong peripheral pulses. Angiography after a year showed a normal axillary artery (Fig. 2).

Discussion

Transient circulatory disturbances after axillary blocks were described earlier,[6,8] and these reversible disturbances

---

B. Ott, MD, L. Neuberger, MD, H.P. Frey, MD, Institute of Anaesthesiology and Intensive Care, University of Bern, Inselspital, 3010 Bern, Switzerland.
Correspondence should be addressed to Dr L. Neuberger please.
Accepted 13 March 1989.

0003–2409/89/090773+02 $03.00/0
© 1989 The Association of Anaesthetists of Gt Britain and Ireland

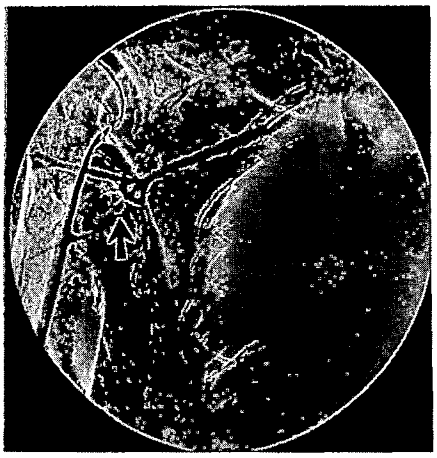


Fig. 1. Angiography of the axillary artery. The arrow indicates the closed segment of the artery.

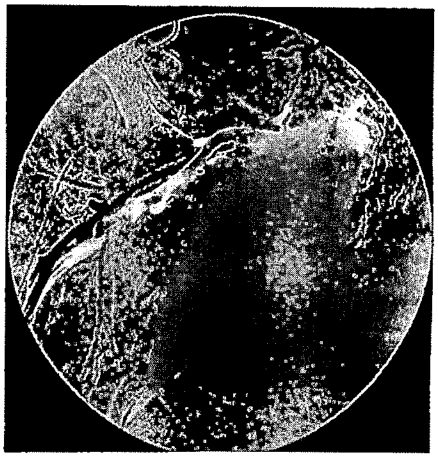


Fig. 2. Control-angiography one year after the operation with a normal patent axillary artery.

can happen after irritation of the vessel wall by the needle, which causes vascular spasm. Compression of the artery by local anaesthetic or vasoconstriction after administration of adrenaline could be other explanations. In this case the needle was accidentally placed intramurally. Injection of a large volume of local anaesthetic caused dissection between the inner layers of the vessels leading to a total obstruction, without the formation of an aneurysm. A similar complication was described by Restelli and coworkers[2] who reported the development of an aneurysm in the axillary vein, which led to venous insufficiency.

The blunt needle technique is a recognised method for an axillary block.[4,5] It is regarded as less traumatic because the blunt needle would probably cause less damage to the nervous structures or to the artery. However, the present case shows that even with this needle and after a normal injection of the local anaesthetic, complications may occur. Skin temperature and the quality of the pulse should routinely be tested and compared to the other arm when the anaesthetic has worn off in order to make an early diagnosis of vascular injury. This is specially important in patients in whom the anatomical structures are difficult to define, as in this patient with obesity, or in those with pathological changes of the vessel walls, such as arteriosclerosis, diabetes and other peripheral vascular diseases. Furthermore, techniques which use arterial puncture before the deposition of local anaesthetic should be used with extreme caution.

References

1. Greene ER. Intravascular injection of local anesthetic after venipuncture of axillary vein during attempted brachial plexus block. *Anesthesia and Analgesia* 1986; **65:** 421.
2. Restelli L, Pinciroli D, Conoscente F, Cammelli F. Insufficient venous drainage following axilliary approach to brachial plexus blockade. *British Journal of Anaesthesia* 1984; **56:** 1051–3.
3. Selander D, Edshage S, Wolff T. Paresthesiae or no paresthesiae? Nerve lesions after axillary blocks. *Acta Anaesthesiologica Scandinavica* 1979; **23:** 27–33.
4. Verlic L, Troxler X. Modifikation der Blockade des Plexus axillaris mit 'Loss of resistance'—Methode mit stumpfer Nadel. *Regional-Anaestesie* 1983; **6:** 36–9. A modification of the axillary plexus block: The 'loss of resistance' method with the ultra short bevel needle. (English title.)
5. Zenz M, Glocker R. Eine neue 'immobile Nadel' zur Plexusanästhesie. *Regional-Anaesthesie* 1981; **4:** 29–31. A new 'immobile needle' for brachial plexus block. (English title.)
6. Lennon RL, Linstomberg JW. Brachial plexus anethesia and axillary sheath elastance. *Anesthesia and Analgesia* 1983; **62:** 215–7.
7. Abramowitz HB, Cohen C. Use of Doppler for difficult axillary block. *Anesthesiology* 1981; **55:** 603.
8. Merrill DG, Brodsky JB, Hentz RV. Vascular insufficiency following axillary block of the brachial plexus. *Anesthesia and Analgesia* 1981; **60:** 162–4.

Anaesthesia, 1989, Volume 44, pages 775–777

CASE REPORT

Epidural anaesthesia and thrombocytopenia

P. HEW-WING, S. H. ROLBIN, E. HEW AND D. AMATO

Summary

A case is presented of a mother with unanticipated profound thrombocytopenia who received a continuous epidural anaesthetic for labour. No neurological sequelae or excessive bleeding occurred. It is clear, after a review of the literature, that more information is needed to define the lower limits of platelet count at which it is safe to proceed with epidural anaesthesia.

Key words

Anaesthetic techniques, regional; epidural.
Complications; thrombocytopenia.

It is commonly accepted that a bleeding tendency is an absolute contraindication to epidural anaesthesia. One authority recommends that epidural analgesia be avoided in patients with a low platelet count.[1] The author suggests a platelet count of 100×10^9/litre as a lower safe limit in patients with pre-eclamptic toxaemia, but for healthy patients no specific number is given. A review of the common reference texts of regional anaesthesia reveals no clear guidelines.[2-4] Mild thrombocytopenia (platelet count $< 150 \times 10^9$/litre) during pregnancy is common, and an incidence of up to 9% has been reported in peripartum women.[5-7] This is a report of a patient with unanticipated profound thrombocytopenia who received an epidural without neurologic complications.

Case history

A 41-year-old black woman, gravida 5, para 4, at full term requested an epidural for analgesia during labour. The pregnancy was normal with no prior history of hypertension, diabetes, bleeding tendency or neurological deficit. No oedema, rash, petechiae, or overt bleeding were seen. Her arterial blood pressure on admission was 130/90 mmHg and she had a trace of protein in her urine (membranes were ruptured), but subsequent blood pressures were all in the normal range (110/80 mmHg). An epidural catheter was inserted at the L_{4-5} space without any difficulty and an epidural block started with 0.25% bupivacaine. The catheter was introduced on the first attempt, passed into the epidural space easily without paraesthesia, and no blood or cerebrospinal fluid was seen. Laboratory results were not available, apart from urinalysis, at the time of epidural insertion.

The patient had good analgesia for 45 minutes at which time she passed a clot of blood (approximate size 250 ml) *per vaginam* and the fetus showed deep sustained variable decelerations to 60 beats/minute. She was promptly delivered vaginally with the use of a vacuum technique followed by an outlet forceps. The baby was healthy, required no resuscitation and had Apgar scores of 8 and 9 at 1 and 5 minutes respectively.

Results from a haematological profile, after the delivery, which were sent on admission, showed that the haemoglobin was 98 g/litre and the platelet count 2×10^9/litre. Repeat testing on the same machine (Coulter Counter model S plus 3, Coulter Electronics Inc., Hialeah, Florida) at the time of delivery, or 2 hours after admission, revealed a haemoglobin of 61 g/litre and platelet count 2×10^9/litre. The blood was deliberately drawn from an arm which had no intravenous infusion. A third sample drawn 2.5 hours after admission was sent to a separate laboratory using a different cell counter (Coulter Counter model S plus 4) and it revealed a haemoglobin of 54 g/litre and a platelet count 4×10^9/litre.

Examination of the blood film revealed large platelets associated with a marked reduction in numbers and no clumping. Red blood cell morphology showed anisocytes, a few spherocytes but no fragments. The reticulocyte count was $> 4\%$ and a prothrombin time, partial thromboplastin time and fibrinogen level were normal. The direct antiglobulin (Coomb's) test was positive. Bone marrow examination revealed hypercellularity of all haemopoietic

---

P. Hew-Wing, MD, FRCP(C), Clinical Fellow, S. H. Rolbin, MDCM, FRCP(C), E. Hew, MD, FRCP(C), D. Amato, MD, FRCP(C), Consultants, Departments of Anaesthesia and Medicine, Mount Sinai Hospital, 600 University Avenue, Toronto, Ontario, Canada M5G 1X5.

Accepted 29 March 1989.

0003–2409/89/090775+03 $03.00/0 © 1989 The Association of Anaesthetists of Gt Britain and Ireland

cell lines which included megakaryocytes. The patient remained stable in the immediate postpartum period, and the epidural catheter was removed without complication. She recovered from the epidural block without neurological deficit and remains neurologically normal 8 months after delivery.

The patient is being followed postpartum by a haematologist. Initially, there was a good response to prednisone and danazol therapy, and the platelet count and haemoglobin returned to normal within a month of delivery. However, with a reduction of the prednisone dose, the thrombocytopenia recurred without anaemia. She is currently taking prednisone 50 mg daily and danazol 200 mg three times a day, and the most recent platelet count is 111×10^9/litre. The diagnosis after 5 months is Evans' syndrome, a coexistence of idiopathic thrombocytopenic purpura and auto-immune haemolytic anaemia. There have been minor nosebleeds during this time but no major bleeding episodes.

Discussion

A platelet count of $150\text{–}400 \times 10^9$/litre is generally accepted as normal, but the same may not be true during pregnancy. Romero[8] reviewed 14 papers that looked at the change in platelet count during pregnancy compared to the nonpregnant state. In his review, five showed a decrease in platelet count, three an increase and six no change. Many,[5,7] despite the controversy, have defined thrombocytopenia during pregnancy as a platelet count below 150×10^9/litre. We measured platelet counts in 1621 randomly selected healthy periparturient patients and showed an incidence of 6.4% of thrombocytopenia as defined above.[5] Ninety-seven patients (6.0%) had platelet counts between 100 and 150×10^9/litre and seven (0.4%) were below 100×10^9/litre. Thrombocytopenia during pregnancy is of concern because a low platelet count may increase the risk to both mother and fetus. It is of particular importance to anaesthetists because thrombocytopenia during labour may increase the risk of an epidural haematoma after epidural anaesthesia.

Neurological deficits secondary to a spontaneous epidural haematoma occur rarely.[9,10] Anecdotal reports suggest there is an increased risk of spontaneous epidural haematoma formation with systemic anticoagulation.[11,12] It is assumed that the risk is even higher if epidural anaesthesia is performed in a patient who is anticoagulated. This may be true if the patient is anticoagulated after the epidural catheter is inserted or if the epidural catheter is removed while the patient is still anticoagulated.[13–15] A review of 36 case reports of paraplegia or paraparesis after epidural anaesthesia showed that there were three patients in whom epidural haematomata were clearly implicated, and in all three cases they had been anticoagulated.[16] However, Rao and El-Etr[17] inserted continuous epidurals in 3164 patients who were subsequently anticoagulated (one hour after insertion of epidural catheter) for lower extremity peripheral vascular surgery. There was no clinical evidence of epidural or subdural spinal cord compression in any of these patients. It seems that epidural catheter insertion is relatively safe in this situation. The precautions taken included confirmation of a normal baseline-activated clotting time and the cancellation of surgery if 'frank blood' was aspirated at initiation of the epidural. The patients were also assessed in the postoperative period for any neurological deficits.

We have found no case report of a thrombocytopenic patient who developed an epidural haematoma after epidural anaesthesia. This may be because physicians avoid epidural anaesthesia in thrombocytopenic patients, or because the cases were not reported. One report describes a healthy patient who developed temporary paralysis after a continuous epidural; the paralysis resolved spontaneously after 6 weeks.[18] The diagnosis of epidural bleeding was made clinically without radiographic or surgical confirmation, but the platelet count was not reported.

Altered platelet function may also increase the risk of neurological sequelae. A spontaneous epidural haematoma occurred after aspirin use,[19] and spinal subdural haematomata were reported in eight thrombocytopenic patients ($1.5\text{–}60 \times 10^9$/litre) with leukaemia who received diagnostic lumbar punctures.[20] Interestingly, only three were symptomatic (paraplegia and cauda equina syndrome), while the other five were detected on autopsy.

It is generally agreed that automated platelet counts are less reliable when the true count is low than when it is normal.[21,22] There are several reasons for this. First, the coefficient of variation is inversely proportional to the number of particles counted, and thus becomes very large when the number of particles counted is small. Second, automated counters have a 'background' or 'noise' level equivalent to a platelet count of $2\text{–}3 \times 10^9$/litre. Third, automated counters tend to overestimate the platelet count in thrombocytopenic specimens, because they may recognise as platelets certain other particles (e.g. erythrocyte or leucocyte fragments, erythrocyte inclusions, etc.).

However, these factors are of little relevance in profound thrombocytopenia ($< 10 \times 10^9$/litre) such as in our patient. The coefficient of variation has little practical importance, since a platelet count of 8×10^9/litre is almost as alarming as one of 2×10^9/litre, despite the 400% difference; repeated counts ranged between 2 and 4×10^9/litre in our patient so worry about overestimation was unnecessary. Underestimation may occur if platelets are clumped or they become attached to leucocytes (platelet satellitism), but these are relatively rare occurrences. Moreover, in our laboratory as in most others, markedly abnormal platelet counts are verified by inspection of a stained blood film or manual counting or both, and this was done in our patient.

Our patient had profound thrombocytopenia without clinical evidence of bleeding. There were no technical difficulties when the catheter was inserted into the epidural space. However, the outcome might have been different if a blood vessel had been traumatised. Current practice demands that a known platelet count of $2\text{–}3 \times 10^9$/litre is an absolute contraindication to epidural analgesia. In addition it is commonly accepted that epidural analgesia is contraindicated in patients with low platelet counts ($< 100 \times 10^9$/litre). It is our practice, however, not to wait for the platelet count before proceeding with epidural analgesia, especially if the patient is very uncomfortable, gives no history of a bleeding tendency, has no illness and is taking no drug which may lower the platelet count or affect platelet function. Herein lies a dilemma. It is clear that the history and physical examination is not enough to detect all cases of profound thrombocytopenia. Ideally we should wait for the platelet count in all labouring patients, but if this were done many would be denied pain relief for a significant time.

The current belief, that epidural anaesthesia is contraindicated in patients whose platelet counts are below 100×10^9/litre, has no supporting data. It is possible that the 'safe platelet count limit' is considerably lower, depending perhaps on platelet function. Our patient is without sequelae after 8 months, but the authors do not wish to imply that it is safe to do epidural anaesthesia at such low levels of platelet count. We do believe, however, that it is safe to proceed with epidural anaesthesia without knowledge of the platelet count in a patient who is healthy and has no bleeding tendency as indicated by the history. Our clinical practice and experience with more than 80 000 epidurals has substantiated this belief. Coagulation studies need be done only if clinically warranted.

References

1. Bromage PR. Neurologic complications of regional anesthesia for obstetrics. In: Shnider SM, Levinson G, eds. *Anesthesia for obstetrics,* 2nd edn. Baltimore: Williams and Wilkins, 1987: 320.
2. Bonica JJ. Spinal (lumbar) epidural block. In: *Principles and practice of obstetric analgesia and anesthesia.* Philadelphia: F.A. Davis, 1969: 611–21.
3. Cousins MJ. Epidural neural blockade. In: Cousins MJ, Bridenbaugh PO, eds. *Neural blockade in clinical anesthesia and management of pain.* Philadelphia: J.B. Lippincott, 1980: 176–274.
4. Moore DC. Single dose and continuous (intermittent) epidural (peridural) block. *Regional block,* 4th edn. Springfield, Illinois: Charles C. Thomas, 1973: 407–38.
5. Rolbin SH, Abbott D, Musclow E, Papsin F, Lie LM, Freedman J. Epidural anesthesia in pregnant patients with low platelet counts. *Obstetrics and Gynecology* 1988; **71:** 918–20.
6. Rasmus KT, Rottman RL, Kotelko DM, Wright WC, Stone JJ, Rosenblatt RM. Unrecognized thrombocytopenia and regional anesthesia in parturients; a retrospective review. Annual report: Meeting for the Society of Obstetric Anesthesia and Perinatology 1987. p. 103.
7. Burrows RF, Kelton JG. Incidentally detected thrombocytopenia in healthy mothers and their infants. *New England Journal of Medicine* 1988; **319:** 142–5.
8. Romero R, Duffy TP. Platelet disorders in pregnancy. *Clinics in Perinatology* 1980; **7:** 327–48.
9. Markham JW, Lynge HN, Stahlman GEB. The syndrome of spontaneous spinal epidural hematoma. Report of three cases. *Journal of Neurosurgery* 1967; **26:** 334–42.
10. Lougheed WM, Hoffman HJ. Spontaneous spinal extradural hematoma. *Neurology* 1960; **10:** 1059–63.
11. Sreerama V, Ivan LP, Dennery JM, Richard MT. Neurosurgical complications of anticoagulant therapy. *Canadian Medical Association Journal* 1973; **108:** 305–7.
12. Spurny OM, Rubin S, Wolf JW, Wu WQ. Spinal epidural hematoma during anticoagulant therapy. Report of two cases. *Archives of Internal Medicine* 1964; **114:** 103–7.
13. Helperin SW, Cohen DD. Hematoma following epidural anesthesia: report of a case. *Anesthesiology* 1971; **35:** 641–4.
14. Butler AB, Green CD. Haematoma following epidural anaesthesia. *Canadian Anaesthetists' Society Journal* 1970; **17:** 635–9.
15. Gingrich TF. Spinal epidural hematoma following continuous epidural anesthesia. *Anesthesiology* 1968; **29:** 162–3.
16. Kane RE. Neurologic deficits following epidural or spinal anesthesia. *Anesthesia and Analgesia* 1981; **60:** 150–61.
17. Rao TLK, El-Etr AA. Anticoagulation following placement of epidural and subarachnoid catheters: an evaluation of neurologic sequelae. *Anesthesiology* 1981; **55:** 618–20.
18. Ballin NC. Paraplegia following epidural analgesia. *Anaesthesia* 1981; **36:** 952–3.
19. Locke GE, Giorgio AJ, Biggers SL, Johnson AP, Salem F. Acute spinal epidural hematoma secondary to aspirin-induced prolonged bleeding. *Surgical Neurology* 1976; **5:** 293–6.
20. Edelson RN, Chernik NL, Posner JB. Spinal subdural hematomas complicating lumbar puncture. Occurrence in thrombocytopenic patients. *Archives of Neurology* 1974; **31:** 134–7.
21. Dalton WT, Bollinger P, Drewinko B. A side-by-side evaluation of four platelet-counting instruments. *American Journal of Clinical Pathology* 1980; **74:** 119–34.
22. Mayer K, Chin B, Magnes J, Thaler T, Lotspeich C, Baisley A. Automated platelet counters. A comparative evaluation of latest instrumentation. *American Journal of Clinical Pathology* 1980; **74:** 135–50.

Anaesthesia, 1989, Volume 44, pages 778–782

Forum

Epidural versus general anaesthesia for elective Caesarean section

Effect on Apgar score and acid-base status of the newborn

C. M. Evans,* MRCP, Clinical Research Fellow, J. F. Murphy,† MRCP, Consultant Neonatologist, O. P. Gray, FRCP, Professor, Department of Child Health, M. Rosen, FFARCS, Professor, Department of Anaesthesia, University of Wales College of Medicine, Heath Park, Cardiff CF4 4XW.

Summary

Elective Caesarean section deliveries over a 5-year period were studied to compare the effect of epidural block with general anaesthesia on the condition of the infant at birth. The Apgar score and umbilical arterial acid-base status were used as determinants of the latter. Epidural block was used in 139 (22.8%) mothers while 471 (77.2%) were performed under general anaesthesia. No babies in the epidural group were severely depressed (Apgar < 4), compared with 6.2% in the general anaesthesia group. Only 4.3% of the epidural sections were moderately depressed (Apgar 4–6), compared with 15.4% of the others. These differences remained highly significant when infants of less than 2500 g were excluded, and when matched groups were compared. Mean umbilical arterial pH was similar within the two groups (pH 7.28), and was not consistent with asphyxia in almost 90% of the depressed infants. The findings suggest that general anaesthesia, rather than asphyxia or aortocaval compression, is responsible for most of the depressed infants born by elective Caesarean section. This may involve over 20% of babies delivered in this manner, so greater use of epidural block for elective Caesarean section is recommended. Further investigations are required to improve results with general anaesthesia.

Key words

Anaesthesia; obstetric, Caesarean section.
Anaesthetic technique, regional; epidural.

One in 10 infants is delivered by Caesarean section, either electively or as an emergency procedure. The principal purpose of a Caesarean section is to deliver the baby in as good or better condition than when the decision to operate is taken. However, the Cardiff Birth Survey[1] revealed that elective Caesarean section in South Glamorgan residents during the period 1970–79 resulted in 9.1% of babies born with a one-minute Apgar score of less than 4, and a further 30.4% with a score of 4–7. Thus four in every 10 infants were in unsatisfactory condition at birth. The figures remained statistically significant after infants who weighed less than 2500 g and those who presented by the breech were excluded. It was recommended that the techniques used for anaesthesia during elective Caesarean delivery be reviewed.

Epidural block for Caesarean section delivery has increased in popularity amongst obstetricians, anaesthetists and mothers alike during the past decade, so that now in many maternity units about half of the elective sections performed are under regional block.[2] Several studies have reported maternal benefits,[3–6] and others comment on a lower incidence of respiratory depression in the newborn when compared with general anaesthesia.[5,7–10] However, opinion remains divided on whether epidural block offers any real advantage over general anaesthesia to mother or baby during elective Caesarean delivery.

This study compares the effect of epidural block with general anaesthesia on the condition of the infant at birth after elective Caesarean section delivery.

Methods

The epidural rate for elective Caesarean section at the University Hospital of Wales increased from less than 1% in 1978 to 32% during the first 6 months of 1985. There was a fivefold increase in epidural sections during 1980 compared with the previous 2 years, marking the time at which epidural block became well established for this mode of delivery in Cardiff. Therefore, all elective Caesarean deliveries performed at the University Hospital of Wales from 1 January 1980 until 30 June 1985 were included in this study.

The mother's name, age, parity, date of delivery, reason for Caesarean section, and details of the anaesthetic administered were obtained retrospectively from the labour ward records, together with the baby's sex, birth weight, and the one- and 5-minute Apgar scores. Information where necessary, was also retrieved from the mother's case notes or from the Cardiff Birth Survey database.

The condition of the infant at birth was assessed according to two criteria, namely the one-and 5-minute Apgar scores and the acid-base status of umbilical arterial

---

*Present address: Department of Paediatric Gastroenterology, St Bartholomew's Centre for Clinical Research, Dominion House, Bartholomew Close, London EC1A 7BE.

†Present address: Department of Neonatology, The National Maternity Hospital, Holles Street, Dublin 2.

Accepted 2 February 1989.

0003–2409/89/090778+05 $03.00/0 © 1989 The Association of Anaesthetists of Gt Britain and Ireland

Table 1. One- and 5-minute Apgar scores compared with mode of anaesthesia: all infants, and 'previous section only' infants.

	All infants		Previous Caesarean section only*	
	General ($n=467$)	Epidural ($n=139$)	General ($n=176$)	Epidural ($n=72$)
One-minute Apgar				
1–3	29 (6%)	0 (0%)	7 (4%)	0 (0%)
4–6	72 (15%)	6 (4%)	25 (14%)	0 (0%)
7–10	366 (79%)	133 (96%)	144 (82%)	72 (100%)
5-minute Apgar				
1–3	8 (2%)	0 (0%)	1 (0.6%)	0 (0%)
4–6	19 (4%)	0 (0%)	8 (4.4%)	0 (0%)
7–10	444 (94%)	139 (100%)	167 (95%)	72 (100%)

*All infants that weighed less than 2500 g excluded.

blood. Umbilical arterial and venous blood specimens have been collected routinely at both elective and emergency Caesarean section deliveries in Cardiff since 1977. The technique used involves double-clamping the umbilical cord at the moment of delivery, and obtaining samples by immediate puncture of vessels in the isolated segment of cord using preheparinised syringes. This method of sampling has been described elsewhere,[11] and is both simple and accurate. All measurements were performed on an acid-base laboratory (Radiometer Copenhagen ABLC) as soon as possible after collection. The cord blood gas data were obtained retrospectively from the records of the Department of Medical Biochemistry.

All anaesthetic procedures were performed by experienced anaesthetists. Patients in the general anaesthesia group received a 50% nitrous oxide:50% oxygen mixture, combined with a halogenated agent in low concentration (halothane or enflurane). Bupivacaine 0.5% plain (without adrenaline) was used for epidural anaesthesia, and the surgeon was allowed to start when the level of block had reached T_{5-6}. Mothers in the epidural group were given supplemental oxygen (50%) through a facemask during the procedure.

Statistical comparisons between the two study groups were performed using standard Chi-squared tests, with a continuity correction factor when indicated; p values of < 0.05 were considered significant.

Results

Elective Caesarean section deliveries were performed on 610 mothers during the study period chosen, of which 139 (22.8%) were under epidural block, and 471 (77.2%) under general anaesthesia. None of the women studied was in labour.

Table 1 compares the infant's Apgar score at one and 5 minutes with the type of anaesthesia. The individual Apgar scores have been grouped into severely depressed (Apgar 1–3), moderately depressed (Apgar 4–6), and vigorous (Apgar 7–10).

In the general anaesthetic group, 6.2% of infants were severely depressed at one minute, whereas there were none in the epidural group (Chi-squared 7.75; df 1; $p < 0.01$). A further 15.4% of these infants were moderately depressed, compared with 4.3% of the epidural group (Chi-squared 10.80; df 1; $p < 0.01$). Thus 21.6% of the general anaesthetic babies had one-minute Apgar scores of less than 7, five times more than those sectioned under epidural block (Chi-squared 20.90; df 1; $p < 0.0001$). These differences remain highly significant when infants that weigh less than 2500 g are excluded; only 4.5% of the epidural group were depressed (Apgar < 7), compared with 20.5% of the general anaesthesia group.

The principal indication for an elective section was previous Caesarean delivery; this had occurred in 176 (37.3%) patients in the general anaesthesia group, and in 72 (51.8%) of those delivered under epidural block. Other indications included malpresentation, diabetes mellitus, placenta praevia, pre-eclampsia, poor obstetric history, multiple pregnancy, maternal illness, rhesus haemolytic disease, cephalopelvic disproportion, postmaturity, high fetal head, and pelvic abnormalities. The most important factor that influenced the decision to section was used if more than one indication was present. Women submitted to section purely because of a previous Caesarean delivery were separated into 'previous section only' groups. None of these patients was in labour, none had any complicating obstetric factors, and all infants that weighed less than 2500 g were excluded.

The one- and 5-minute Apgar scores in the two 'previous

Table 2. Umbilical artery acid-base data: all infants and 'previous section only' infants.

	All infants		Previous Caesarean section only*	
	General ($n=471$)	Epidural ($n=139$)	General ($n=176$)	Epidural ($n=72$)
Number with cord gases	412	125	161	68
% with cord gases	87.5%	90.0%	91.5%	94.4%
Mean umbilical art pH	7.28	7.28	7.28	7.29
(SD)	(0.05)	(0.05)	(0.04)	(0.04)
Range of values	7.09–7.37	7.05–7.40	7.13–7.37	7.16–7.40
Mean base deficit	−4.4	−4.7	−4.3	−4.1

*All infants that weighed less than 2500 g excluded.

Table 3. Relationship between one-minute Apgar score, umbilical arterial pH, and mode of anaesthesia.

	All infants		Previous Caesarean section only*	
	General ($n=412$)	Epidural ($n=125$)	General ($n=161$)	Epidural ($n=68$)
Asphyxiated (Apgar <7, pH <7.20)	11 (2.7%)	1 (0.8%)	3 (1.8%)	0 (0%)
Depressed (Apgar <7, pH >7.20)	78 (18.9%)†	2 (1.6%)†	26 (16.1%)†	0 (0%)†
Acidotic but vigorous (Apgar >7, pH <7.20)	5 (1.2%)	5 (4.0%)	2 (1.2%)	2 (3%)
Normal (Apgar >7, pH >7.20)	318 (77.2%)	117 (93.6%)	130 (80.9%)	66 (97%)

*All infants that weighed less than 2500 g excluded.
†$p<0.0001$.

section only' cohorts are also shown in Table 1. Both groups are matched for maternal age and parity, together with the infant's birth weight and sex. No significant differences were detectable between these factors. There were no babies in the epidural group with an Apgar of less than 7 at one or 5 minutes. However, 18.2% of general anaesthesia infants were depressed at one minute (Chi-squared = 13.46; df 1; $p < 0.001$), 4.0% of them severely; a further 5.1% remained depressed at 5 minutes (Chi-squared = 7.04; df 1; $p < 0.01$).

Cord blood gas data for the main and 'previous section only' groups are shown in Table 2. Full results were available in 87.5% of the general anaesthesia group, and in 90.0% of the epidural group. These infants were almost identical in the distribution of their one- and 5-minute Apgar scores to the study group as a whole. The mean umbilical arterial pH and range in both general anaesthesia and epidural cohorts were similar (7.28, SD 0.05). Samples were available in 91.5% of general anaesthesia and 94.4% of epidural groups in the 'previous section only' babies. The mean umbilical arterial pH was again similar, at 7.28 (SD 0.04) and 7.29 (SD 0.04) respectively, very similar to that of all infants studied. Mean umbilical arterial base deficit varied only marginally between groups.

Cord blood acid-base data were unavailable in a small number of infants. No samples were obtained in some, or they had clotted or contained air bubbles. It was not possible to distinguish the venous from the arterial sample in a few, and the results from these infants were excluded.

The relationship between one-minute Apgar score and umbilical arterial pH is shown in Table 3. Eighty-nine of the 412 infants in the general anaesthetic group with cord blood gas data had one-minute Apgar scores of <7 (21.6%). However, the umbilical arterial pH was less than 7.20 ($\times 2$ SD from the mean) in only 11 of these. Thus 87.6% of the depressed babies in the general anaesthesia group showed no evidence of asphyxia (Apgar < 7, pH $>$ 7.20). This accounts for 18.9% of the total general anaesthesia group, compared with only 1.6% (2/125) of the total epidural group (Chi-squared 21.38; df 1; $p < 0.0001$). A similar picture was seen in the 'previous section only' groups.

Discussion

The increase in the use of epidural block for elective Caesarean section deliveries in Cardiff in the 5 years studied, from less than 2% to over 30%, reflects growing popularity in this method of anaesthesia in obstetrics generally. However, opinion remains divided over whether regional block offers any real advantage over general anaesthesia to both mother and baby during elective section delivery.

Apgar[8] was amongst the first to report that babies delivered by Caesarean section under spinal block were, in general, more vigorous at birth than those whose mothers had cyclopropane. Several workers report a marginal improvement in one-minute Apgar scores in infants delivered by Caesarean section under epidural block,[5,7,8–10] but others have found no difference.[12–15] Most studies have involved small numbers, with usually less than 20 in each group. However, larger studies[9,10,16] have suggested that respiratory depression amongst newborns may be up to fivefold greater with general anaesthesia compared with epidural block. Gale *et al.*[16] studied 531 emergency and elective Caesarean deliveries, 242 performed under general anaesthesia and 289 under epidural. A significantly lower incidence of neonatal respiratory depression (Apgar < 7) was reported for the epidural group as a whole, although cord blood gas data were available in only 27 of the elective sections, in whom there was no difference in respiratory depression between the two anaesthetic groups. Morgan[17] reported an extremely low incidence of depressed Apgar scores amongst elective Caesarean section deliveries at Queen Charlotte's Maternity Hospital in 1984, where the epidural rate for 200 normal singletons that weighed more than 2500 g was 94%. Our study demonstrates a highly significant difference in the frequency of depressed one-minute Apgar scores between the two techniques of anaesthesia, with a fivefold increase amongst the general anaesthesic group.

Obstetric complications can have a profound influence upon the infant's condition, and these may also play a decisive role in the selection of anaesthesia. Therefore, a matched cohort of patients was chosen in an attempt to eliminate as many complicating obstetric factors as possible. Only women undergoing an uncomplicated elective section because of previous Caesarean delivery were selected. None was in labour, and all malpresentations and infants that weighed less than 2500 g were excluded. The results remained highly significant, and confirmed that respiratory depression was lower in the epidural than the general anaesthetic group (0% cf. 18.2%).

Cord blood acid-base analysis revealed similar results for arterial pH and base deficit in all study groups. Mean values in each are comparable with other series and are well within the range considered normal. Almost 90% of the depressed infants had arterial pH values above 7.20 and thus showed no biochemical evidence of birth asphyxia. Therefore, respiratory depression after elective Caesarean delivery was not due to asphyxia in these babies, and was almost exclusively confined to infants delivered under general anaesthesia (78/80, Chi-squared 21.38; df 1; $p < 0.0001$). An unexpected finding concerned the group of acidotic, but vigorous infants (Apgar > 7, pH < 7.20), in whom there was a slightly higher percentage of babies in the total epidural group compared with the total general anaesthesia group (4% cf. 1.2%). The numbers involved are very small, however, and the difference between the two groups is not statistically significant ($p > 0.1$). Fetal acidosis may have resulted from unrecognised maternal hypotension that occurred during induction of anaesthesia, which is potentially more of a problem with regional block. None of these infants, in the event, required any form of resuscitation at birth.

Several studies have shown a direct correlation between respiratory depression and prolongation of the induction–delivery interval during inhalational anaesthesia. Stenger[18] demonstrated a 54% incidence of respiratory depression amongst infants in whom mean duration of exposure to nitrous oxide was 36 minutes, compared with 15% when it was 15 minutes. Shnider[10] reported similar figures; the incidence of Apgar scores above 6 decreased from 74% to 36% when mean duration of nitrous oxide anaesthesia increased from less than 10 minutes to greater than 30 minutes. Nitrous oxide appears to be the agent most liable to cause neonatal depression.[10] The general anaesthetics given to our patients, as mentioned previously, consisted of a 50% nitrous oxide:50% oxygen mixture combined with a halogenated agent in low concentration (halothane or enflurane), and were administered by experienced anaesthetists.

We did not investigate the induction–delivery interval in any of our study groups, but others have shown that the duration of epidural block has little or no effect on the infant's condition at birth, even if delivery is delayed for over 2 hours.[10] It was demonstrated, however, that a prolonged uterine incision–delivery time during Caesarean section can have a profound effect upon the infant. Intervals that exceed 3 minutes are likely to be followed by respiratory depression secondary to asphyxia.[19] This was unlikely to have been a contributory factor in the depressed babies in this study, 90% of whom had a normal pH.

The high number of depressed Apgar scores observed at one minute in those delivered under general anaesthesia is clearly of concern. The principal purpose of delivering an infant by elective Caesarean section is to ensure minimum risk to the mother, and to optimise the infant's condition. Neonatal resuscitation is not without risk; iatrogenic laryngospasm, trauma to the upper airway, pneumothorax, and tracheal perforation are all recognised hazards.[20,21] The administration of drugs such as oxygen, naloxone, adrenaline and sodium bicarbonate are also potentially dangerous, particularly if the clinician is inexperienced. In addition, an infant who is depressed secondary to anaesthetic agents will develop biochemical changes of asphyxia if apnoea persists for more than a few minutes or resuscitation is ineffectual. This may have accounted for some of the 5.7% of infants still depressed 5 minutes after delivery, in whom umbilical arterial pH and base deficit were normal at one minute.

The maternal benefits of epidural anaesthesia have been well documented by Morgan *et al.*[3] They include less pain and discomfort postoperatively, fewer cases of gastrointestinal stasis, pyrexia and coughing after surgery, earlier mobilisation and breast-feeding, and a lower incidence of postoperative depression. Another study produced similar conclusions,[22] and it has been claimed that complications related to epidural block are generally less serious and easier to manage than those associated with general anaesthesia.[5] Of more significance, inhalational anaesthesia during labour has been consistently recognised as the single most important cause of maternal death, particularly in association with Caesarean section. Concern has also been expressed recently in both the medical and lay press in relation to maternal awareness during general anaesthesia for Caesarean section; several cases resulted in litigation. Finally, epidural block allows the mother to experience childbirth actively; it also makes the father's presence at the delivery more meaningful.

Anaesthetic-induced respiratory depression in the neonate after Caesarean delivery, although usually transient, remains undesirable, since it may interact with other risk factors to affect postnatal outcome adversely.[23,24] The results of this large study suggest that elective Caesarean section delivery under epidural block should be encouraged, and that the techniques used for general anaesthesia in obstetric patients require further investigation, since general anaesthesia remains essential in some cases. It is anticipated that these steps should lead to an improvement in the condition of the infant at birth, lessen the need for active resuscitation, and possibly improve maternal morbidity after Caesarean delivery.

Acknowledgments

We thank The Laerdal Foundation, who provided financial support for C. M. Evans, and the Department of Medical Biochemistry at the University Hospital of Wales for kindly allowing us access to their records.

References

1. MURPHY JF, DAUNCEY M, REES GAD, ROSEN M, GRAY OP. Obstetric analgesia, anaesthesia and the Apgar score. *Anaesthesia* 1984; **39**: 760–3.
2. MOIR DD. *Obstetric analgesia and anaesthesia.* London: Bailliere Tindall, 1980.
3. MORGAN BM, BARKER JP, GOROSZENIUK T, AULAKH JM, REGINALD PW, TROJANOWSKI A. Anaesthetic morbidity following caesarean section under epidural or general anaesthesia. *Lancet* 1984; **i**: 328–30.
4. DAVIS AG. Anaesthesia for Caesarean section: The potential for regional block. *Anaesthesia* 1982; **37**: 748–53.
5. MORGAN BM, AULAKH JM, BARKER JP, GOROSZENIUK T, TROJANOWSKI A. Anaesthesia for Caesarean section. A medical audit of junior anaesthetic staff practice. *British Journal of Anaesthesia* 1983; **55**: 885–88.
6. MOIR DD. Extradural analgesia for Caesarean section. *British Journal of Anaesthesia* 1979; **51**: 79–80.
7. JAMES FM, CRAWFORD JS, HOPKINSON R, DAVIES P, NAIEM H. A comparison of general anaesthesia and lumbar epidural analgesia for elective Caesarean section. *Anesthesia and Analgesia* 1977; **56**: 228–35.
8. APGAR V, HOLADAY DA, JAMES LS, PRINCE CE, WEISBROT IM. Comparison of regional and general anesthesia in obstetrics. With special reference to transmission of cyclopropane across the placenta. *Journal of the American Medical Association* 1957; **165**: 2155.
9. BENSON RC, SHUBECK F, CLARK WM, BERENDES H, WEISS W, DEUTSCHBERGER J. Fetal compromise during elective Cesarean section. A report of a collaborative project. *American Journal of Obstetrics and Gynaecology* 1965; **91**: 645–56.
10. SHNIDER SM, LEVINSON G. *Anaesthesia for obstetrics.* Baltimore: Williams and Wilkins, 1979.
11. SYKES GS, MOLLOY PM, JOHNSON P, GU W, ASHWORTH F, STIRRAT GM, TURNBULL AC. Do Apgar scores indicate asphyxia? *Lancet* 1982; **1**: 494–96.
12. DOWNING JW, HOULTON PC, BARCLAY A. Extradural analgesia for caesarean section: a comparison with general anaesthesia. *British Journal of Anaesthesia* 1979; **51**: 367–73.
13. FISHER JT, MORTOLA JP, SMITH B, FOX GS, WEEKS SK. Neonatal pattern of breathing following caesarean section:

epidural versus general anaesthesia. *Anesthesiology* 1983; **59:** 385–9.

14. Fox GS, Smith JB, Namba Y, Johnson RC. Anaesthesia for caesarean section: further studies. *American Journal of Obstetrics and Gynaecology* 1979; **133:** 15–9.
15. Hollmen AI, Jouppila R, Koivisto M, Maatta L, Pihlajaniemi R, Puukk M, Rantakyla P. Neurologic activity of infants following anesthesia for Cesarean section. *Anesthesiology* 1978; **48:** 350–56.
16. Gale R, Slater PE, Zalkinder-Luboshitz I. Neonatal advantage of epidural anaesthesia in elective and emergency Cesarean sections: a report of 531 cases. *European Journal of Obstetrics Gynecology and Reproductive Biology* 1986; **23:** 369–77.
17. Morgan BM. Obstetric anaesthesia, analgesia and low Apgar score. *Anaesthesia* 1985; **40:** 915.
18. Stenger VG, Blechner JN, Prystowsky H. A study of prolongation of obstetric anesthesia. *American Journal of Obstetrics and Gynecology* 1969; **103:** 901.
19. Datta S, Alper MH, Brown WU. Anaesthesia for caesarean section: Importance of induction-delivery and incision-delivery interval on neonatal outcome. *Abstracts of scientific papers, annual meeting of the American Society of Anaesthesiologists,* Chicago, 1978.
20. Serlin SP, Daily WJR. Tracheal perforation in the neonate: a complication of endotracheal intubation. *Journal of Pediatrics* 1975; **86:** 596–7.
21. Joshi VV, Mandavia SG, Stern L, Wiglesworth FW. Acute lesions induced by endotracheal intubation. Occurrence in the upper respiratory tract of newborn infants with respiratory distress syndrome. *American Journal of Diseases of Childhood* 1972; **124:** 646–49.
22. Sosis W, Bodner A. Is general anaesthesia becoming obsolete for Caesarean section? *Anaesthesia* 1983; **38:** 702–3.
23. Crawford JS, Davies P. Status of neonates delivered by elective Caesarean section. *British Journal of Anaesthetics* 1982; **54:** 1015–22.
24. Evans CM. Risk and the Neonate. In: James DK, Stirrat GM, eds. *Pregnancy and risk: the basis for rational management.* Chichester: John Wiley, 1988: 137–69.

Anaesthesia, 1989, Volume 44, pages 783–794

Correspondence

Dr A.J.H. Hewer: an appreciation 783
L.W. Hall, PhD and B.M.Q. Weaver, PhD
Fentanyl and hypothermia 784
E. Lee, FFARCSI and B. Ben-David, MD
J.H. Smith, MRCP, FCAnaes and M. Parr, MRCP, FCAnaes 784
K.R. Johnston, FFARCS and R.S. Vaughan, FFARCS 784
Propofol infusion for cardiac anaesthesia 785
S. Ghosh, FFARCS and D.W. Bethune, FFARCS
G.N. Russell, FFARCS 785
Bilateral carotid artery thrombosis 785
C.J. Wilkins, FFARCS and M.W.R. Bennett, MB, BS
Sleep apnoea 786
C.D. Hanning, FFARCS
N.M. Tierney, MB, ChB, B.J. Pollard, B.Pharm, FFARCS, and B.R.H. Doran, FFACSR 786
The Replogle tube 787
D.N. Ranasinghe, FFARCS, S. Logan, MB, BS, E.J. Ashcroft, MRCP, MRCGP
Artefactual 'hypotension' from shivering 787
J.G. de Courcy, DA, DCH
C. Eldred 788
Failure of an adjustable pressure limiting valve 788
R.A. Nelson, MRCP and S.L. Snowdon, FFARCS
T.R. Davies 789
The oesophageal detector device 789
C. Ananthanarayan, MD, FRCP
Pulmonary oedema after carbamazepine overdose 789
J.P. Begley, MB
Occlusion of armoured tubes 790
J.M. Hull, MB, ChB
D.G.L. Wood 790
The laryngeal mask in patients with chronic respiratory disease 790
A.I.J. Brain, FFARCSI
Incidence of sore throats with the laryngeal mask 791
C.A. Alexander, FFARCS and A.B. Leach, FFARCS
Bain system for use with a circle absorption 791
C.M. Kumar, FFARCS
Kinked breathing systems—again 792
G.D. Prince, DRCOG, FFARCS and B.J. Nicholls, FFARCS
Anaesthesia for carbon dioxide laser laryngeal surgery in infants 793
R. Williamson, FFARCS
The ethics of difficult tracheal intubation 793
R. Williamson, FFARCS
Anaesthetists as physicians 794
M. O'Connor, FFARCS
R.M. Jones, FFARCS 794
Bad publicity 794
J. Stevens, FFARCS

Dr A.J.H. Hewer: an appreciation

We are deeply saddened to learn of the death of Dr A.J.H. Hewer and are concerned that his role in the development of veterinary anaesthesia in this country should be given proper recognition. We would also like to record our own personal everlasting gratitude to him for his patience in teaching us the importance of good, safe anaesthesia in veterinary surgical practice.

Our first introduction to Dr Hewer, or 'Jan' as we came to know him, was through Mr Handley, Consultant Surgeon at the Middlesex Hospital, who visited the Royal Veterinary College in Camden Town with the Surgeon Travellers' Club. He saw us using cyclopropane with home-made equipment to anaesthetise dogs and suggested that Jan would be able and very willing to help us develop our then rudimentary methods. Soon after this we became regular visitors to the Middlesex to see Jan at work and to learn all that we could from his very skilful practice of anaesthesia for both general and neurosurgery. He also came to our hospital to help us apply his techniques to our animal patients. This was at the exciting time when techniques such as controlled ventilation with neuromuscular blocking agents and controlled hypotension with ganglionic blocking drugs were being developed. He taught us the fundamentals of modern anaesthesia and awareness of possible complications while he instilled his enthusiasm and concern for every detail of patient care.

Jan was also directly instrumental in the formation of the Association of Veterinary Anaesthetists of Great Britain and Ireland: he arranged for us to meet his colleague Dr O.P. Dinnick who then gave so much assistance in its early, formative years. In recognition of his services to veterinary anaesthesia Jan was elected an Honorary Member but, regrettably, ill health prevented his attendance at many meetings of the Association.

University of Cambridge
University of Bristol,
Langford House,
Bristol BS18 7DU

L.W. Hall
B.M.Q. Weaver

All correspondence should be addressed to Dr J. N. Lunn, Editor of *Anaesthesia*, Department of Anaesthetics, University Hospital of Wales, Heath Park, Cardiff CF4 4XW, United Kingdom.

Letters must be typewritten on one side of the paper only and double spaced with wide margins. Copy should be prepared in the usual style and format of the Correspondence section. Authors must follow the advice about references and other matters contained in the Notice to Contributors to *Anaesthesia* printed at the back of each issue. The degrees and diplomas of each author must be given in a covering letter personally signed by all the authors.

Correspondence presented in any other style or format may be the subject of considerable delay and may be returned to the author for revision. *If the letter comments on a published article in Anaesthesia, please send three copies; otherwise two copies of your letter will suffice.*

Fentanyl and hypothermia

We were interested to read the report by Johnston and Vaughan (*Anaesthesia* 1988; **43:** 1024–5) in which they present a case of postoperative hypothermia and coma, in a patient with long standing diabetes insipidus, undergoing fundoplication through a left thoracoabdominal incision. We are puzzled as to why the authors choose to dismiss the overdose of epidural fentanyl as a possible aetiological factor. Instead, the events in this case are attributed to 'subclinical pituitary dysfunction'. They base their conclusion on the evidence that hypothalamic lesions are known to be associated with impaired thermoregulation, and that 'three other patients who had thoracotomies in the same theatre suite did not develop a similar degree of hypothermia' (though none of them received a similar dose of fentanyl). We take issue with their conclusions, and believe there is a good body of evidence, both clinical and pharmacological, to implicate the epidural fentanyl as the prime suspect.

Fentanyl is unique on account of its high dural permeability, which facilitates its entry into the CSF.[1] The patient in the report received a large dose, high volume injection of epidural fentanyl (300 μg in 25 ml over 40 minutes) at the T_{5-6} interspace. This would have almost certainly resulted in high intracranial levels, levels perhaps so high that 400 μg of intravenous naloxone was insufficient to reverse its effect. Therefore, it is not surprising that this patient exhibited prolonged unconsciousness. We do not dispute that the hypothermia became a contributing factor to the unconsciousness. What we do dispute is the aetiology of the hypothermia.

There is substantial evidence to support the contention that the hypothermia resulted from high intracranial levels of fentanyl. Body temperature regulation is controlled by the thermoregulatory centre located in the pre-optic hypothalamus.[2] It is well known that opioid agonists act on the thermoregulatory centre to change body temperature in animals.[2,3] The direction, magnitude and time course vary with a number of factors including route of administration, ambient temperature and restraint of the animal. A dose-dependent 'dual response' (low dose, hyperthermia and high dose, hypothermia) occurs in the rat, mouse and primates.[2] The exact mechanisms involved in body temperature changes produced by morphine are not established. Possible mechanisms of morphine-induced hypothermia include decreased metabolic heat production, centrally mediated suppression of shivering thermogenesis and peripheral vasoactive effects which result in redistribution of body heat.[2,4] Small doses of intravenous opioids were used successfully to treat shivering after general[5] and epidural anaesthesia[6] without any significant change in body temperature. Johnson *et al.*[4] reported a patient who received a large dose of epidural sufentanil (100 μg) to control pain and shivering after epidural anaesthesia for Caesarean section. Pain and shivering were abolished rapidly, but at the expense of a profound decrease in body temperature (35°C to 33°C) despite active rewarming. Their report lends further support to the implication of high dose epidural narcotics in the causation of hypothermia.

We fail to see how Drs Johnston and Vaughan can reasonably conclude that hypothermia and coma in their patient resulted from pituitary dysfunction. This patient underwent a laparotomy several years earlier with no such complication. Moreover, the diagnosis reached by Drs Johnston and Vaughan is one of exclusion, yet they have failed to exclude the most likely cause for the hypothermia and instead have concluded that this is the first such reported case of hypothermia from subclinical pituitary dysfunction. We therefore find their conclusion untenable, and think it inappropriate for them to suggest that patients with diabetes insipidus are at increased risk from hypothermia on the basis of this report. This most interesting case does suggest that the effects of (high dose?) spinal narcotics on body temperature warrant further investigation.

Bnai Zion Medical Center,
P.O. Box 4940
Haifa 31048
Israel

E. Lee
B. Ben-David

References

1. Bullingham RES, McQuay HJ, Moore RA. Principles of use of extradural and intrathecal narcotics. In: Kaufman L, ed. *Anaesthesia Review 2*. Edinburgh: Churchill Livingstone, 1984: 137–47.
2. Adler MW, Geller EB, Rosow CE, Cochin J. The opioid system and temperature regulation. *Annual Review of Pharmacology and Toxicology* 1988; **28:** 429–49.
3. Spencer RL, Hruby VJ, Burks TF. Body temperature response profiles for selective mu, delta and kappa opioid agonists in restrained and unrestricted rats. *Journal of Pharmacology and Experimental Therapeutics* 1988; **246:** 92–101.
4. Johnson MD, Sevarino FB, Lema MJ. Cessation of shivering and hypothermia associated with epidural sufentanil. *Anesthesia and Analgesia* 1989; **68:** 70–1.
5. Pauca AL, Savage RT, Simpson S, Roy RC. Effect of pethidine, fentanyl and morphine on postoperative shivering in man. *Acta Anaesthesiologica Scandinavica* 1984; **28:** 138–43.
6. Casey WF, Smith CE, Katz JM, O'Loughlin K, Weeks SK. Intravenous meperidine for control of shivering during caesarean section under epidural anaesthesia. *Canadian Journal of Anaesthetics* 1988; **35:** 128–33.

We were interested to read Drs Johnston and Vaughan's report (*Anaesthesia* 1988; **43:** 1024–5) of delayed recovery from anaesthesia. We accept that there may be an element of hypothalamic dysfunction in this case, but we find it hard to dismiss such a large dose of epidural fentanyl as only a contributory factor. Epidural narcotics have been implicated in postoperative hypothermia[1] and if the core temperature, which was not measured, was 32°C the patient may well have been too cold to shiver when given naloxone.[2] There is good evidence that intravenous naloxone would have reversed the respiratory depression without affecting analgesia significantly.[3]

Southmead General Hospital,
Bristol BS10 5NB

J.H. Smith
M. Parr

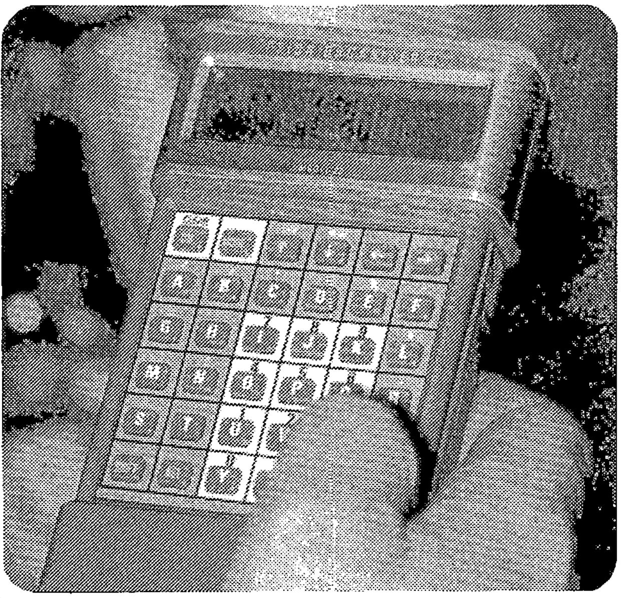
References

1. Johnson M, Sevarino F, Lema, MJ. Cessation of shivering and hypothermia associated with epidural sufentanyl. *Anesthesia and Analgesia* 1989; **68:** 70–1.
2. Slotman GJ, Jeh, Burchard KW. Adverse effects of hypothermia in postoperative patients. *American Journal of Surgery* 1985; **149:** 495–501.
3. Rawal N, Schott U, Dahlstrom B, Inturrisi CE, Tandon B, Sjostrand U, Wennhager M. Influence of naloxone infusion on analgesia and respiratory depression following epidural morphine. *Anesthesiology* 1986; **64:** 194–201.

A reply

We thank Drs Lee, Ben-David, Smith and Parr for their comments on our case report and take the opportunity to answer some of the points raised.

There was no anaesthetic record available from the



Synchro Soft

AUDIT OUT OF CHAOS

NOW!!!

A unique flexible system ideal for all Anaesthetic Departments. Providing both Administrative & Outcome Audit.

- ***Quick and simple to use.***
- ***Absolutely no paper-work.***
- ***Rapid access to stored information.***
- ***Low, viable expenditure.***
- ***NCEPOD compatible.***

For detailed information or demonstration of the **Hospital Audit System** contact:-

Denise Chamberlain
Product Information Manager
Synchro Soft
Red Lion Cottage
Catforth
Preston PR4 0HE

Synchro Soft

FINAL F.C.Anaes. EXAM
INTENSIVE COURSE, BRISTOL

THE BRISTOL CRAMMER

11–15 DECEMBER 1989

This five-day course will include tutorials on intensive care, current topics, practical subjects (viz. ECGs, X-rays, equipment and examination of clinical cases. Sessions will be conducted by national and local experts and will include mock examinations and performance analyses

For further details, please contact:

The Secretary, Dept. of Anaesthesia,
Bristol Maternity Hospital,
Southwell Street, Bristol BS2 8EG
Telephone: (0272) 215411 ext 204

Course Director: DR DAVID COATES F.C.Anaes.

COURSE FEE £160

FLUID RESUSCITATION

(Baillières Clinical Anaesthesiology)

EDITORS: **W. Kox** *Dept Anaesthesia, Charing Cross and Westminster Medical School, London, UK*

J. Gamble *Dept Physiology, Charing Cross and Westminster Medical School, London, UK*

THIS practical, research-based reference book not only covers the wide range of topics that need to be addressed during the management of patients in shock, but also considers the rationale for their implementation.

Up-to-date reviews include new approaches in resuscitation, e.g. the development of artificial O_2 carriers and the use of low volume hyperosmotic, hyperoncotic resuscitation techniques. The ongoing discussion, crystalloid versus colloid fluid replacement, is considered. The cardiovascular effects of fluid administration as well as the rationale for the use of ionotropic and vasoactive drugs following fluid loading are examined. Likewise, the effect of protein metabolism and fluid balance and its implications on parenteral nutrition during the process of fluid resuscitation is discussed. Problems arising from fluid replacement therapy such as reperfusion injury, the administration of particulate contaminants, plasma substitutes and the interference of these substances with blood grouping are addressed as well as the prevention and treatment of fluid overload. This book caters for the requirements of specialists in intensive care, anaesthetists as well as physicians and surgeons who are interested in understanding and thereby pre-empting shock-related injury.

Contents

PATHOPHYSIOLOGY AND PRINCIPLES OF FLUID RESUSCITATION:

J. Gamble - The principles governing microvasculature transendothelial fluid exchange
A. Kirkman & R.A. Little - The pathophysiology of trauma and shock
S. J. Machin - Disturbances of haemostasis in surgical and critically ill patients
M.I.M. Noble - Cardiovascular response to fluid loading
J.L. Vincent - A rationale for the use of inotropic and vasoactive drugs during fluid loading

FLUID REPLACEMENT THERAPY:

U. Kreimeier & K. Messmer - Fluid replacement in shock
W. Shoemaker - Crystalloid versus colloid fluid resuscitation
E.S. Parry - The use of blood products in the treatment of hypovalaemia and shock
D. Denison - Artificial oxygen carriers
A. Fleck - Nutrition, protein metabolism and fluid balance

SEQUELAE AND SIDE-EFFECTS OF FLUID RESUSCITATION:

D. Royston - Reperfusion injury
W. Kox - Influence of plasma substitutes on blood typing and cross matching
H. Hesselvick & B. Brodin - Reticulo-endothelial response to administration of plasma substitutes
C.N. McCollum - The use of microfilters in fluid resuscitation
T.A. Golper - Treatment of the overhydrated patient in the ITU

0 7020 1340 4 ca 230pp Hb June 1989 Baillière Tindall £18.50

Baillière Tindall

Available from your local bookseller. Prices, specifications and availability are subject to change without prior notice. For further information please contact: Marketing Department, Harcourt Brace Jovanovich Ltd, 24-28 Oval Road, London NW1 7DX, UK.

previous surgical procedure because this was undertaken in another centre. However, it may not be relevant since hypothalamic dysfunction may not have been present at that time.

The dose of epidural fentanyl (300 μg), although large in our practice, was administered nearly 3 hours before the end of surgery at a site from which systemic uptake and dural penetration is known to be rapid. In a similar case, the full details of which cannot be presented, when a similar dose of epidural fentanyl was inadvertently administered, it was our clinical impression that both the respiratory depression and analgesia were rapidly reversed by a 400-μg intravenous bolus of naloxone. Both were reversed, so this does not agree fully with the paper by Rawal *et al.* Further, neither delayed recovery nor an unusual decrease in body temperature occurred. The paper by Johnson *et al.* and the review by Adler *et al.* were unfortunately not published at the time of preparation of our report (see references in Drs Lee and Ben-David, and Smith and Parr).

We accept, in the light of the recent increase in the body of knowledge on the effects of opioids on temperature regulation, the suggestion made by Drs Lee and Ben-David that the large epidural dose of fentanyl, although not directly responsible for the prolonged coma, may have played a contributory role in the occurrence of central hypothermia in our patient. However, with a proven association between hypothalamic dysfunction and hypothermia we still suggest caution when patients known to suffer from this group of conditions are anaesthetised and that core temperature is monitored and that all practical measures are taken to minimise heat loss during surgery.

University Hospital of Wales,
Cardiff CF4 4XN
K.R. Johnston
R.S. Vaughan

Propofol infusion for cardiac anaesthesia

We were interested in the description of the use of propofol by infusion for cardiac surgery by Russell *et al.* (*Anaesthesia* 1989; **44:** 205–8) and suggest that some caution may be necessary with the dosage regimen that they suggest. We assessed alternative anaesthetic techniques to replace the trichloroethylene-based method successfully used at Papworth for the last 20 years, since the loss of the product licence for that agent. One of the techniques involved the use of an opiate premedication (papaveretum 0.3 mg/kg); a midazolam (0.03 mg/kg) fentanyl (15 μg/kg) induction with a propofol infusion for maintenance of anaesthesia (3 mg/kg/hour). This level of propofol infusion is much lower than that used by Russell *et al.*, but we have had to reduce the infusion rate to correct hypotension in a number of patients with good pre-operative ventricular function scheduled for coronary artery bypass grafting.

Our dose of propofol is lower than that required to maintain anaesthesia when used as a sole agent, but in combination with midazolam and fentanyl appears to give satisfactory anaesthesia with no recollection of intra-operative events on direct questioning after operation. There were in addition no signs of intra-operative sympathetic overactivity with the exception of some hypertensive response to sternotomy which could be readily controlled by sodium nitroprusside.

We consider that propofol by infusion may be suitable for cardiac surgical patients, but our experience with low infusion rates suggests that the higher fixed rates proposed by Russell *et al.* may not be appropriate; the infusion rate may need to be tailored to the individual patient and in addition it would appear that the rates selected by Russell *et al.* may be greater than that necessary to ensure effective hypnosis and amnesia for the operative period.

Papworth Hospital,
Cambridge CB3 8RE
S. Ghosh
D.W. Bethune

A reply

A two-stage fixed rate infusion was used in our study to define more clearly the alteration in blood propofol concentration with the onset of specific events such as cardiopulmonary bypass (CPB), hypothermia and rewarming. Indeed, anaesthesia was supplemented in one patient by the addition of enflurane, rather than alteration of the infusion rate as would be normal clinical practice. Our study was large enough to define the trends in propofol concentration, but we were careful to warn against extrapolation of dose range requirement from a small series of relatively young patients (mean age 53 years). In our continued clinical use of propofol, our loading infusion rate is often reduced, particularly in the elderly, and the infusion rate varied to achieve haemodynamic stability in the pre- and post-bypass period.

Assessment of depth of anaesthesia is virtually impossible during CPB, so we continue to use a fixed rate infusion of 3 mg/kg/hour. The minimum infusion rate (MIR) of propofol supplemented with moderate dose fentanyl has yet to be determined formally. The communication from Drs Ghosh and Bethune further supports our clinical experience that the relatively low infusion rate of 3 mg/kg/hour, supplemented in this way, reliably provides hypnosis and amnesia during cardiopulmonary bypass.

Royal Liverpool Hospital,
P.O. Box 147,
Liverpool L69 3BX
G.N. Russell

Bilateral carotid artery thrombosis

We report a case of bilateral carotid artery thrombosis caused by attempted self-hanging; there is a need to maintain a high index of suspicion for this complication of blunt trauma to the neck.

An 18-year-old man attempted to commit suicide by jumping from scaffolding with a noose around his neck. The knot slipped and he fell 20 ft to the ground. He managed to crawl to the site office and make himself a cup of tea and was discovered about 6 hours later.

He was fully conscious with no abnormal neurological signs on arrival at the Accident and Emergency Department. There was bruising around the neck consistent with the history. X rays showed a complete fracture through the base of the odontoid peg with anterior displacement of the atlas on the axis. Skull X rays were normal but there were bilateral fractures of the femora.

The patient's level of consciousness rapidly deteriorated while he was in the A and E department and he suffered a respiratory arrest. His trachea was immediately intubated and controlled ventilation begun. Extensor posturing of the left side with normal movement on the right was noted at this time. Cervical traction via a skull halo was applied under general anaesthesia and the patient transferred to the intensive care unit, where he was sedated and paralysed.

Twenty-four hours after admission he developed an intermittently dilated and unreactive right pupil. A CT scan showed a large area of low density within the right cerebral hemisphere, consistent with infarction. The patient's condition deteriorated and he died the next day. Postmortem examination revealed complete occlusion of the right internal carotid artery by thrombus and laceration and thrombosis of the left common artery, together with infarction of most of the right cerebral hemisphere.

It is recognised that carotid artery occlusion may follow blunt trauma to the neck[1,2] and there may be a considerable delay in the onset of symptoms.[3] The slow evolution of symptoms and signs may focus attention on spurious diagnoses; in this case we assumed that the neurological deterioration was caused by cerebral hypoxia at the time of the respiratory arrest, or as a result of a blow to the head during the fall.

Other authors have reported successful treatment of this complication by exploration of the affected vessels following angiography[3] and it may be that the outcome in this case would have been different had the neurosurgical and orthopaedic surgeons and anaesthetists involved been more aware of the problem.

General Infirmary,
Leeds LS1 3EX

C.J. Wilkins
M.W.R. Bennett

References

1. Hughes JT, Brownwell B. Traumatic thrombosis of the internal carotid artery in the neck. *Journal of Neurology Neurosurgery and Psychiatry* 1968; **31:** 307–14.
2. Little JM, May J, Vanderfield GK, Lamond S. Traumatic thrombosis of the internal carotid artery. *Lancet* 1969; **2:** 926–30.
3. Yamada S, Kindt GW, Youmans JR. Carotid artery occlusion due to nonpenetrating injury. *Journal of Trauma* 1967; **7:** 333–42.

Sleep apnoea

The report by Tierney, Pollard and Doran (*Anaesthesia* 1989; **44:** 235–7) of a patient with obstructive sleep apnoea (OSA) deserves further comment. The most important omission from the report is the severity of the OSA. It can be presumed from the presence of polycythaemia and right ventricular failure that the patient was either of Grades 2 or 3, that is the most severe form of the condition.[1] Such patients do not cope well with surgery, as is well illustrated by this report. The nocturnal hypoxaemia should be corrected by nasal continuous positive airway pressure (CPAP) or tracheostomy and the cardiac status permitted to stabilise before surgery. Protryptilline has no place in the management of OSA of this severity and limited use in milder forms.[2]

Premedication should be avoided for fear of precipitating prolonged apnoea.[3] Nasal packing is very dangerous for such patients and the nose should be packed around nasopharyngeal tubes to which CPAP may be applied if necessary. The observation that the patient had episodes of central apnoea does not imply any central nervous system deficit but is a reflection of the rebound excessive Stage 4 and rapid eye movement sleep after relief of the OSA by the tracheal tube.[4,5]

The exquisite sensitivity to opioids shown by this patient suggests that the nasal surgery was not sufficient to abolish his OSA. This a common clinical finding in long standing cases and emphasises the necessity for repeated overnight sleep studies in patients with severe problems.

Patients with severe OSA present a considerable problem to the anaesthetist and correct management is important if a crisis is to be avoided. The choice of tracheostomy or nasal CPAP may be difficult and such patients are probably best managed in those centres that have the necessary expertise and equipment. The moves by the British Thoracic Society to promote the development of Sleep Disorders Clinics are thus to be welcomed. The experience of treating over 300 patients in the last 6 years has convinced the writer that the anaesthetist has many skills relevant to this field and that we should increase our involvement.

Leicester General Hospital,
Leicester LE5 4PW

C.D. Hanning

References

1. Lugaresi E, Mondini S, Zucconi M, Montagna P, Cirignotta F. Staging of heavy snorers' disease: A proposal. *Bulletin Européen de Physiopathologie Respiratoire* 1983; **19:** 590–4.
2. Sanders MH. Nonsurgical management of snoring and obstructive sleep apnea. In: Fairbanks DNF, Fujita S, Ikematsu T, Simmons FB, eds. *Snoring and obstructive sleep apnea.* New York: Raven Press, 1987: 79–100.
3. Craddock M, Lees DE. Anesthesia for obstructive sleep apnea patients: risks, precautions and management. In: Fairbanks DNF, Fujita S, Ikematsu T, Simmons FB, eds. *Snoring and obstructive sleep apnea.* New York: Raven Press, 1987: 235–43.
4. Issa FG, Sullivan CE. The immediate effects of nasal continuous positive airway pressure treatment in patients with obstructive sleep apnea syndrome. *Electroencephalography and clinical neurophysiology.* 1986; **63:** 10–7.
5. Hanning CD. Obstructive sleep apnoea. *British Journal of Anaesthesia.* 1989; **61:** (in press).

A reply

We agree that this patient suffers from severe cardiorespiratory disease but the proportion due to his chronic obstructive lung disease and that caused by his obstructive sleep apnoea, is difficult to define. One could predict that he might require postoperative ventilation on the evidence of the arterial blood gases alone.[1]

We also agree that these problematical individuals are best dealt with by units with knowledge and expertise in this expanding field. The gentleman in question was under the care of such a unit here in Manchester, and was referred to us by that unit.

The best treatment for this patient is debatable. To the extent that his presenting complaint of daytime hypersomnolence was cured, one could argue that the minimalist approach taken was the optimum in this case. Tracheostomy is obviously a tempting alternative, but as we discussed in the case report, this operation in patients with obstructive sleep apnoea and chronic obstructive lung

NORWICH ANAESTHETIC STUDY DAY

SATURDAY, 28TH OCTOBER, 1989.

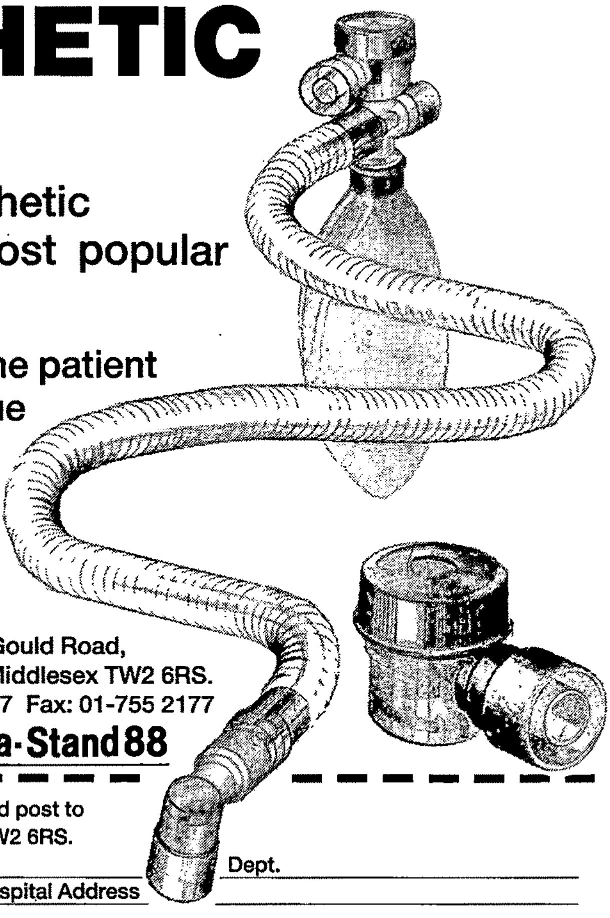
-MORNING SESSION-

"EXEMPLARY PAIN RELIEF BY OPIATES"

-AFTERNOON SESSION-

"PAEDIATRICS AND ANAESTHESIA FOR THE D.G.H."

APPLICATION FORMS FROM MRS. JUDITH LEA, ADMINISTRATOR, N.A.N.I.M.E., NORFOLK AND NORWICH HOSPITAL, NORWICH, NR1 3SR OR TELEPHONE JUDITH LEA - (0603) 628377 EXT: 3576.



THE ANAESTHETIC CONNECTION

A new range of disposable anaesthetic breathing systems covering the most popular Mapleson configurations.

- Lightweight – preventing "pull" on the patient connection and anaesthetist's fatigue
- Completely disposable – including reservoir bag, breathing system and valve – eliminating all possibility of cross infection

INTERSURGICAL
COMPLETE RESPIRATORY SYSTEMS

Crane House, Gould Road,
Twickenham, Middlesex TW2 6RS.
Tel: 01-755 1477 Fax: 01-755 2177

See us at the Annual Association·Swansea·Stand 88

For further information on our new range please fill in the coupon and post to Intersurgical, Crane House, Gould Road, Twickenham, Middlesex TW2 6RS.

Name ____ Position ____ Dept. ____
Hospital ____ Hospital Address ____
Currently using ____

Seminars in Anesthesia

Editor:
RONALD L. KATZ

Editorial Board
Richard J. Kitz, Emanuel M. Papper, John J. Bonica,
Werner Flacke and A.H. Giesecke, Jr.

Publication: Quarterly
Subscription: Volume 8, 1989
Institutions: £60.00 (UK)/$91.00 (Overseas)

Seminars in Anesthesia will provide the anesthesiologist with a review of important topics in the field. Each issue will be devoted to an area of particular importance in which invited experts will discuss a wealth of clinical experience. All practising anesthesiologists will find *Seminars* a source of current and reliable information.

From a recent issue

Anesthesia for the Asthmatic Patient, *Ronald Dueck*
Thoracic Anesthesia, *Roger S. Wilson*
Anesthesia for Airway Surgery, *John V. Donlon, Jr*
Anesthesia for the Sickle Cell Diseases and Other Hemoglobinopathies, *Jeff Ray Gibson, Jr*
Anesthesia for Orthopedic Surgery, *Ralph L. Bernstein and Andrew D. Rosenberg*
Clinical Immunology of Chemonucleolysis, *Anna Uitvlugt and Jonathan Moss*
Clinical Aspects of Chemonucleolysis, *Joseph O. Reagan and Howard L. Zauder*
Anesthesia for Extracorporeal Shock Wave Lithotripsy, *David Gissen*

Coupon

Seminars in Anesthesia

To: Journals Marketing Department
Academic Press Ltd
24–28 Oval Road
London NW1 7DX, England

Please tick

☐ Please send me a sample copy and subscription details of *Seminars in Anesthesia*

Signature.. Name (Capitals) ....

Address ....

.... Date..........................

disease may lead to more prolonged periods of desaturation.

Continuous positive airways pressure applied nasally, may be advantageous, but we are unaware of any data on its use in this subgroup of patients. We would be interested if Dr. Hanning does have evidence of the success of this approach in patients with cor pulmonale and obstructive sleep apnoea, because this would herald a significant advance in the management of these difficult patients.

Reference

1. MILLEDGE JS, NUNN JF. Criteria of fitness for anaesthesia in patients with chronic obstructive lung disease. *British Medical Journal* 1975; **3:** 670–3.

Manchester Royal Infirmary,
Manchester M13 9WL

N.M. TIERNEY
B.J. POLLARD
B.R.H. DORAN

The Replogle tube

We wish to report the use of a Replogle tube in a 4-year-old girl admitted to the Intensive Care Unit with aspiration pneumonia secondary to bulbar palsy later found to be due to Guillain-Barré syndrome. This use of a Replogle tube is not already described as far as we are aware.

The patient had weak cough and gag reflexes on admission, was only able to whisper, had left-sided ptosis and no swallowing reflex, a left twelfth nerve palsy and right-sided pneumonia.

The trachea was intubated with a 5.0-mm nasotracheal Portex tube for 10 days. Her chest cleared and she was able to breathe air comfortably after the first few days. The trachea was extubated, but she produced copious secretions which obstructed her airway. The secretions had to be removed using a Yankauer sucker every few minutes to maintain a patent airway. Both the airway obstruction and the suction of secretions caused much distress to the child. Intravenous hyoscine was used in an attempt to reduce the production of secretions but had no effect.

Nasogastric feeding was commenced and since she had no swallowing reflex the other methods for the protection of her airway from secretions and regurgitated feeds were either the prolonged use of a tracheal tube or a tracheostomy. In view of the serious side effects associated with these two alternatives, especially in a child of this age, it was decided to try a Replogle tube to aspirate her secretions with suction continuously. Replogle tubes are routinely used in the pre-operative management of tracheo-oesophageal fistula in neonates.[1]

The tube was constructed as follows. One centimetre was cut off the end of a size 16-F gauge Levin's tube. A size 5-F gauge suction catheter was threaded through a hole bored 14 cm from the end of the Levin's tube until its tip was at the level of the holes in the Levin's tube. The larger tube was connected to the suction apparatus while the 5-F gauge catheter was connected to the administration set of a 500-ml bag of 0.9% saline, the continuous flow from which helped to keep the holes in the larger tube patent.

The tube was then passed through the child's nose into her pharynx and, by trial and error, the position at which secretions were best aspirated was determined. A silk suture was very firmly bound round the tube to mark the level of her nostril to facilitate re-insertion.

The presence of this modified Replogle tube enabled this child with no swallowing reflex to remain conscious, breathe spontaneously and maintain her airway and avoided the need for re-intubation or tracheostomy. This method seemed to work well. However, the tube obstructed with secretions every 3 days or so and needed replacement.

This modified Replogle tube is suggested as a means of aspirating saliva in patients with bulbar palsy, possibly as an alternative to tracheal intubation or tracheostomy, especially in children in whom the hazards of these procedures can be severe.

Sunderland District Hospital,
Sunderland SR4 7TP

D.N. RANASINGHE
S. LOGAN
E.J. ASHCROFT

References

1. HATCH DJ, SUMNER E. *Current topics in anaesthesia series: Neonatal anaesthesia and perioperative care.* London: Edward Arnold, 1986.

Artefactual 'hypotension' from shivering

Hypotension and shivering after epidural blockade in obstetric anaesthetic practice are common. The use of automated oscillotonometric blood pressure devices in labour wards is frequent, and two recent cases have emphasised the need to interpret their readings with caution, since at first false diagnoses of hypotension were made.

A normotensive 23-year-old primigravida with a term twin pregnancy was admitted in early labour and epidural analgesia was requested. An intravenous preload of 1000 ml compound sodium lactate solution was commenced. A Datascope Accutorr 1A oscillotonometric blood pressure monitor was attached to her right arm and a baseline reading of 121/75 mmHg was recorded. An epidural catheter was placed at the second lumbar interspace, as the patient lay in the left lateral position, and a test dose of 2.5 ml 2% lignocaine was given. Thereafter automated blood pressure readings were repeated at frequent intervals. When the possibility of subarachnoid block was excluded after a delay of 10 minutes, and there was no change in the blood pressure, a dose of 7 ml 0.5% bupivacaine was injected and an epidural infusion of 0.125% bupivacaine was commenced.

The patient started to shiver violently after several minutes and during this episode the machine reading of the Accutorr was 63/30 mmHg with a pulse rate of 134/minute. The machine did not show any artefact or malfunction warnings. The fetal heart rates were unchanged and the patient reported no subjective symptoms of hypotension. The rate of the intravenous infusion was immediately increased, but before ephedrine was given the pulse was checked and found to be 65/minute. Immediate auscultation of Korotkoff sounds in the left arm revealed a blood pressure of 120/70 mmHg. Another Accutorr reading with the patient still shivering was 70/42 mmHg, pulse 127/

minute, again with no malfunction warning. Simultaneous manual measurement of the blood pressure was 120/65 mmHg.

Five minutes later the shivering abated and thereafter the recordings made by the machine agreed with those made manually. A normal epidural block to T_{10} developed. The pressures in both arms were checked at this point and found to be the same by Korotkoff sounds. The Datascope subsequently showed accurate function when it was checked on two normotensive subjects.

Several days later the author witnessed an identical sequence of events in a different maternity unit with the same model of Datascope Accutorr: again the common features were violent shivering and concurrent falsely low blood pressure reading; no malfunction indicators were displayed.

The machines presumably interpreted the shivering as arterial impulses, and the pattern of the shivering imitated the increase and decrease of pulsations of a normal measuring cycle, and thus prevented the activation of the artefact warnings. Awareness of this potential misdiagnosis of epidural-induced hypotension may prevent the unnecessary and potentially dangerous administration of fluids and ephedrine to a normotensive patient.

Poole General Hospital,
Poole BH15 2JB
J.G. de Courcy

A reply

It is possible to read blood pressure values by shivering. If the size of noise made by the shivering is larger than that of arterial impulses, the machine cannot recognise pulsation during a normal measuring cycle and records false readings.

The Accutorr stops bleed-down during an inversion of pressure. Sequential noises, such as the shivering, which are level with arterial impulses do not cause the inversion of pressure and also they are not recognised as artefact. The Accutorr 1A/2A recognises 2 to 8 mmHg peaks (variable according to the pressure sampling) of pressure as artefact. If Accutorr detects the same level pulsation with noises, a measurement is not carried out and a warning indicator is displayed. However measurements, such as mentioned above, are not always recognised as measurement failures.

It is thus necessary to take measurements on shivering subjects with caution. The amplitude of each oscillotonometric pulsation recorded in 'verify' format should be confirmed in order to avoid misdiagnosis and compared with that in normal measurement cycle.

Datascope Medical Co Ltd,
Cambridge Science Park,
Cambridge CB4 4WE
C. Eldred

Failure of an adjustable pressure limiting valve

In November 1988 a new gas scavenging system was installed at the Royal Liverpool Hospital by Ohmeda including Adjustable Pressure Limiting (APL) valve units (Part No. 1368877). A feature of these units is the inclusion of a secondary blow-off valve after the expiratory valve to prevent breathing system pressure from increasing above 1.0 kPa in the event of occlusion of the scavenging pipe. In addition there is a pressure limit valve set to 7.0 kPa to protect the breathing system even when the APL valve is fully screwed down.

Shortly after their introduction three of the valves failed to close, although they were apparently screwed shut. This occurred in a Mapleson A breathing system which was checked before use at start of the list. The fault happened on one occasion in the middle of the list, after satisfactory function in two previous patients.

Examination of the valves from two of these incidents revealed the same fault. The plastic valve disc had become tilted on its spindle, the edge of the disc had caught on its metal seating and the valve was held open (Fig. 1). Attempts to close the valve by turning the top resulted in the disc being more firmly wedged against its seating. If the top was unscrewed the disc loosened and could return to its proper position.

When one of the valves was dismantled it was clear that the valve disc and spindle were constructed from one piece of translucent plastic and that at the fully closed position, approximately 9 mm of spindle protruded beyond its housing. The spindle was flexible and easily allowed the valve disc to tilt. The valve disc itself had in addition a roughened edge, although it is not known whether this was cause or effect of the valve impacting on its seat. Roughness of the inner aspect of the valve housing was implicated previously in valve malfunction,[1] but this did not appear to be the case with our valve: the sides were quite smooth.

All the three valve failures occurred after the administration of a muscle relaxant and resulted in inability to ventilate the patients' lungs. This was, on each occasion, corrected by substitution of a new breathing system or a new valve, but not always before the patient had become cyanosed.

Such incidents are examples of a not uncommon anaesthetic problem, that is, failure to ventilate the patient.

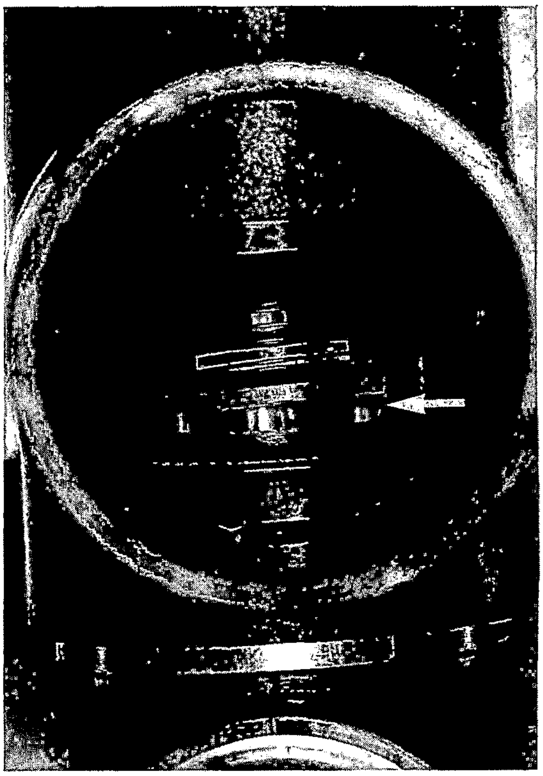


Fig. 1. View along scavenging port of 'closed' APL valve, showing valve disc tilted.

When confronted with a problem unexpectedly the precise cause may not be apparent for a number of reasons. The source of the sound caused by a leak may be obscured by other noises (e.g. alarms, scavenging or air conditioning systems) or even muffled by the attachment of the gas scavenging exhaust system.

Obviously, the careful pre-anaesthetic checking of all equipment is of utmost importance,[2] but some faults cannot be prevented and for this reason a 'failure to ventilate' drill is to be commended.

The three general sites of failure which need considering are: where the patient and breathing system meet (mask or tracheal tube); the breathing system itself; or the anaesthetic machine. If the fault is not obvious but is suspected to be in the breathing system then we recommend exchanging the entire system for another, rather than a search for the precise source of the failure. If the problem is not corrected by this manoeuvre then the patient should be ventilated with a self inflating bag and anaesthesia maintained if necessary with intravenous agents. The breathing system and anaesthetic machine can then be examined *later* rather than risk a futile search whilst the patient is left attached to faulty equipment and ventilated inadequately.

All the APL valves of the type described have been withdrawn from service at our hospital as advised by Ohmeda. We would be interested to hear if others have had similar problems.

Royal Liverpool Hospital,
P.O. Box 147,
Liverpool L69 3BX

R.A. Nelson
S.L. Snowdon

References

1. Personal communication, Ohmeda.
2. Cundy J, Baldock GJ. Safety check procedures to eliminate faults in anaesthetic machines. *Anaesthesia* 1982; **37:** 161–9.

A reply

Ohmeda welcomes the opportunity to discuss the clinical application of its products with clinicians and is pleased to respond to the comments made by Drs Nelson and Snowdon.

The APL Valve (part number 1368877) referred to is designed for in-line use such as a Magill system. The valves concerned were not available for examination, but others were tested in an attempt to duplicate the reported problem. The results show that only when the valve disc and spindle are displaced is it possible to hold the valve open when it is apparently screwed shut.

We agree that careful pre-anaesthetic checking of all equipment is of utmost importance. It is by means of such a check-out that the integrity of the breathing system can be verified before use.

This is especially important where components of the breathing system can be mishandled during cleaning and assembly. Ohmeda considers that the APL valve is safe and effective for its intended use, provided it is not damaged and is used in accordance with the operating instructions.

Ohmeda,
Harlow,
Essex CM19 5AB

T.R. Davies

The oesophageal detector device

Dr Wee's article on this device (*Anaesthesia* 1988; **43**; 27–9) and the correspondence from Dr Nunn (*Anaesthesia* 1988; **43:** 804) prompted me to use this device. Its simplicity, ease of use and almost 100% reliability is impressive: I have used a disposable bulb syringe (Pharmaseal Labs) in 100 cases with a 15-mm adaptor which connects on to the tracheal tube.

The device is particularly useful when working with medical students and I was able to detect oesophageal intubation, subsequently verified by laryngoscopy, in every single case of its occurrence. This device has special application outside the operating room, in the emergency room, intensive care unit ward, and inside ambulances where tracheal intubations are often done by doctors and personnel who may not have much experience.

The end tidal CO_2 monitor is claimed to be the most sensitive for the detection of oesophageal intubation, however it may give false positive readings in the first few seconds because of the presence of gas in the oesophagus. This device works more quickly than the CO_2 monitor, which is not always available, and has potential application in third world countries.

Mount Sinai Hospital,
600 University Avenue,
Toronto, Ontario, M5G 1X5,
Canada

C. Ananthanarayan

Pulmonary oedema after carbamazepine overdose

In their case report, Kitson and Wauchob (*Anaesthesia* 1988; **43:** 967–9) attribute the development of pulmonary oedema to the ingestion of carbamazepine, and believe the antidiuretic properties of the drug to be sufficient in overdose to produce the observed complication. The data presented, however, do not support their theory.

The antidiuretic action of carbamazepine is sufficient to implicate the drug in the 'Syndrome of the Inappropriate Antidiuretic Hormone secretion' (SIADH),[1] though measurement of ADH in these situations has shown appropriate suppression of serum levels.[2] This suggests that carbamazepine either has inherent antidiuretic activity or potentiates the action of ADH. Retention of water with retention of proportionally less solute is the net effect, with resultant dilution of body fluids. This is characterised biochemically by a reduction in serum levels of sodium and, often, urea. Hyponatraemia is a regular feature of carbamazepine therapy, and sodium levels in serum have been shown to correlate negatively with both dose[3] and serum level of carbamazepine.[4] The antidiuretic effect is of rapid onset[3] and would be expected to be a feature of an acute overdose. However, in the reported case, neither of the expected biochemical changes referred to are a feature and significant water retention is, therefore, unlikely to have occurred. Contrary to the authors' assertion, low proteins alone cannot be taken as evidence since there are many explanations for a low serum albumin, the most significant protein fraction, in hospital patients.[5]

Case reports of carbamazepine toxicity are indeed rare in the literature, though a recent study of four cases coupled with a review of literature cases attempts to define a characteristic clinical course.[6] The report of this complication is important, but the antidiuretic action of carbamazepine does not appear to be the explanation and other causative mechanisms for the development of pulmonary oedema must be sought.

Royal Infirmary,
Bristol BS2 8HW

J.P. BEGLEY

References

1. SARDILLO P, SAGRANSKY DM, MERCADO R, MICHAELIS MF. Carbamazepine-induced syndrome of inappropriate antidiuretic hormone secretion. Reversal by concomitant phenytoin therapy. *Archives of Internal Medicine* 1978; **138:** 299–301.
2. MEINDERS AE, CEJKA V, ROBERTSON GL. The antidiuretic action of carbamazepine in men. *Clinical Science and Molecular Medicine* 1974; **47:** 289–99.
3. LAHR MB. Hyponatremia during carbamazepine therapy. *Clinical Pharmacology and Therapeutics* 1985; **37:** 693–6.
4. PERUCCA E, RICHENS A. Antiepileptic drugs: clinical aspects. In: Richens A, Marks V, eds. *Therapeutic drug monitoring.* Edinburgh: Churchill Livingstone, 1981.
5. WHICHER J, SPENCE C. When is serum albumin worth measuring? *Annals of Clinical Biochemistry* 1987; **24:** 572–80.
6. WEAVER DF, CAMFIELD P, FRASER A. Massive carbamazepine overdose: clinical and pharmacological observations in five episodes. *Neurology* 1988; **38:** 755–9.

Occlusion of armoured tubes

This is a report of three cases of obstruction of Mallinckrodt, MCC, disposable armoured tracheal tubes.

The three patients were on intensive care units; one was breathing spontaneously through a continuous positive airway pressure system and two were receiving automatic ventilation of the lungs. It is our usual policy to change from armoured to ordinary tracheal tubes on admission to ITU, but in these cases it was deemed appropriate to leave the Mallinckrodt tubes in place because of the presence of either severe head injury, fractured cervical vertebrae or previously difficult intubation. The patients bit down on the tracheal tube, crushed the wire spiral and irreversibly occluded the lumen. All three patients became hypoxic before the crushed tubes could be removed and exchanged for ordinary tracheal tubes.

The problem of obstruction with this particular tube was first reported in 1983,[1] and after that report Mallinckrodt planned to issue a warning that 'a bite block should be used in cases where the patient may bite down on the tube' but this warning is not included with the tube in this country.

The MCC tube is becoming increasingly popular, but anaesthetists should be aware of this potentially life threatening problem, especially since it could not occur with the 'old' nylon reinforced latex tracheal tube.

University Hospital,
Nottingham NG7 2UH

J.M. HULL

Reference

1. MCTAGGART RA, SHUSTACK A, NOSEWORTHY T, JOHNSTON R. Another cause of obstruction in an armoured endotracheal tube. *Anesthesiology* 1983; **59:** 164.

A reply

We are aware of this potential problem, especially following the letter to *Anesthesiology* in 1983 and subsequent response by our USA organisation.

We are reviewing our policies in line with EEC proposals about 'inserts' with our product in a similar manner to the USA. We shall, of course, highlight this matter.

Finally, we have instructed our representatives that when this product is promoted, all anaesthetists should be informed of the possible risk when nonparalysed patients are intubated.

Mallinckrodt,
11 North Portway Close,
Northampton NN3 4RQ

D.G.L. WOOD

The laryngeal mask in patients with chronic respiratory disease

Dr Gunawardene's letter (*Anaesthesia* 1989; **44:** 531) draws attention to a common anaesthetic problem. The difficulty of maintenance of adequate anaesthesia in patients with significant lung disease when inhalational methods are used is well known. However, there is no evidence that the problems described in her letter are caused by the presence of the laryngeal mask (LM).

Unfortunately Dr Gunawardene appears to have misunderstood the papers referred to in her letter.[1,2] It is not the case that muscle relaxants or deep anaesthesia are 'not recommended' when using the LM. It is entirely appropriate to deepen the anaesthetic or even, if need be, to paralyse the patient if problems occur during anaesthesia with the patient breathing spontaneously through a laryngeal mask. If the problem is inadequate depth of anaesthesia it is usually sufficient to increase the concentration of vapour while gently assisting ventilation by hand. Patients with lung disease, the obese and heavy smokers can certainly be managed successfully and safely with the LM if this method is adopted.

Dr Gunawardene is to be congratulated on her successful insertion of the LM in the patient described, since insertion is a stimulus which may indeed provoke some of the problems described if unskillfully carried out. However, experience of using the LM over a number of years indicates that once in place it does not itself act as a strong stimulus and can indeed be left in place until reflexes are restored. It is therefore inappropriate and potentially dangerous to attempt to remove the LM in a patient who is partially anaesthetised, since this may result in loss of the airway, dislodgement of the bite-block (which should always be in place throughout) and damage to the LM.

A thick roll of gauze inserted between the teeth and taped to one side of the LM tube is also satisfactory. It avoids the danger of damage to capped teeth and stabilises the LM. Perhaps one should also think of silent regurgitation if an obese patient suddenly starts to cough during an apparently adequate anaesthetic. A 7-mm tracheal tube can be gently inserted into the oesophagus behind the LM if it is well lubricated. Perhaps this should be considered when using the LM in the obese. Use of the LM by itself is contraindicated in the presence of gastric contents.

10 Preston Drive,
London E11

A.I.J. Brain

References

1. Brain AIJ. The Laryngeal Mask—A new concept in airway management. *British Journal of Anaesthesia* 1983; **55:** 801–5.
2. Alexander CA, Leach AB, Thompson AR, Lister JB. Use your Brain. *Anaesthesia* 1988; **43:** 893.

Incidence of sore throats with the laryngeal mask

Patients tend to judge surgeons not by their skills or the intricacies of the surgery, but by the appearance of the resultant scar. Anaesthetists, if remembered at all, are judged by the absence or presence of postoperative nausea/vomiting, generalised muscle pains, or sore throat.

The laryngeal mask[1] (LM) has probably no effect on nausea and vomiting, a small effect on generalised postoperative muscle pains, (secondary to the reduced need for suxamethonium), but very marked beneficial effects on the occurrence of postoperative sore throat, the evidence for which we now present below.

Three hundred and twenty-one unselected patients who had general surgical, orthopaedic, gynaecological and genitourinary procedures under general anaesthesia were surveyed to ascertain the incidence of sore throats. Patients were anaesthetised by 12 anaesthetists of all grades, all of whom, with one exception, had a minimum of 6 months' experience using the LM. The choice between the LM, tracheal tube (TT) or facemask (FM) was left to the individual anaesthetist, and recovery staff recorded the decision. Each patient was asked the next day about sore throat after operation. The incidence and duration of sore throat was recorded using a simple scale which relates severity to duration (see table) and repeat ward visits made at 24 and 36 hours as necessary. Day case surgery was excluded from the survey.

No attempt was made to relate the occurrence of sore throat to the type or duration of the procedure. However, it should be emphasised that the LM is used routinely by a number of anaesthetists for major or prolonged procedures which may involve intermittent positive pressure ventilation of the lungs.

Table 1. Incidence and duration of sore throat.

	Laryngeal mask	Tracheal tube	Facemask
No sore throat	163 (93%)	54 (51%)	35 (90%)
Mild, <12 hours	13 (7%)	42 (40%)	4 (10%)
Moderate, >12 hours	0	7 (7%)	0
Severe, >24 hours	0	3 (3%)	0
Total 321	176 (55%)	106 (33%)	39 (12%)

We conclude that, in skilled hands, the occurrence of postoperative sore throats is significantly reduced by the use of the LM.

Specific contraindications should be observed. It is interesting that the incidence of sore throat in the LM and FM groups was comparable, which suggests that the inflated cuff of the LM does not cause direct mucosal damage. Would routine humidification of dry inspired gases further reduce the incidence?

Royal East Sussex Hospital,
Hastings,
East Sussex TN34 1ER

C.A. Alexander
A.B. Leach

Reference

1. Brain AIJ. The laryngeal mask—A new concept of airway management, *British Journal of Anaesthesia* 1983; **55:** 801–5.

Bain system for use with a circle absorption system

We read with interest the letter from Drs Sweeney and Tordoff (*Anaesthesia* 1989; **44:** 262–3) about the use of the Lack system with circle absorption system. This is a report of a similar use of the Bain system with circle absorption system.

Numerous variations of the circle arrangement are possible depending on the relative positions of the unidirectional valves, overspill (pop-off) valves, reservoir bag and the site of entry of the fresh gas flow.[1] Economy of fresh gas requires that the reservoir bag and subject should be on opposite sides of the unidirectional valves, that gas inflow must not enter between the subject and the expiratory valve and the overspill valve must not be between the subject and the inspiratory valve.[2] The Lack system was used successfully with the circle system but needed modification in the system described by Sweeney *et al.* Many anaesthetists might prefer to use the Bain system provided that it can be combined with the circle system without modification. The system described is within one of the many variations described in the literature.

The assembly is essentially similar to the Lack addition to the circle system suggested by Sweeney *et al.* A Bain system with its valve in the closed mode is attached to the inspiratory port of the circle system (Ohmeda MK4). The reservoir bag of the Bain system is removed. A 30-cm length of corrugated scavenging tubing is fitted with male 22-mm connectors on both ends. One end is attached to the bag mount of the Bain system and the other to the expiratory port of the circle system. The relief valve on the circle system is kept in open position and the exhaust system is connected for scavenging of the gases.

A Bain system with circle system was used with a minimum 4 litres/minute fresh gas flow for spontaneously breathing patients, and base line respiratory rate, end-tidal carbon dioxide, heart rate, blood pressure and oxygen saturation were noted. A standard Bain system without the circle system was substituted after 20 minutes and supplied with 10 litres/minute flow on the same patients for another 20 minutes. We found no significant change in respiratory rate, end-tidal carbon dioxide, heart rate, blood pressure and oxygen saturation.

This system was also checked with the relief valve of the Bain system in its open position since many anaesthetists might prefer this for safety reasons. There was some venting of expired gases with a fresh gas flow of 4 litres/minute but venting increased as the flow was increased. This will necessitate an extra exhaust connexion.

The lightness and versatility of a coaxial system are combined with economy of low flow and a considerable financial saving may then follow.

South Cleveland Hospital,
Middlesbrough,
Cleveland TS3 4BW

C.M. Kumar

References

1. Conway CM. Anaesthetic breathing system. In: Scurr C, Feldman S, eds. *Scientific foundations of anaesthesia,* 3rd edn. London: Heinemann Medical 1982: 559.
2. Eger EI, Ethans CT. The effects of inflow, overflow and valve placement on economy of the circle system. *Anesthesiology* 1968; **29:** 93–100.

Kinked breathing systems—again

We would like to report a potentially lethal complication of the use of a paediatric intensive care headset (Portex 8.5 mm Infant Ventilation/Breathing System 100/268/000). This system is designed primarily as ventilator tubing which is easily secured to the head in small infants, but conversion to an Ayre's T-piece is possible if a gas supply is attached to one end and an open-ended bag is attached to the other.

A 3.8-kg male baby with bronchiolitis was admitted to ITU on the sixth day of illness after deterioration of his condition. His trachea was intubated through the nose and intermittent positive pressure ventilation of the lungs was started with a Servo 900B connected to the patient by a Portex headset. Chest percussion combined with deep assisted ventilation was effective in loosening sputum plugs and was performed frequently using the Ayre's T-piece conversion of the headset. The expiratory tubing became kinked on one occasion, during turning, at the headband (Fig. 1, point C). Despite rapid correction of the problem and the use of a small fresh gas flow (3.5 litres/minute) the child developed bilateral tension pneumothoraces and extensive surgical emphysema. Chest drains were inserted and full recovery eventually occurred.

The use of silicon rubber tubing, which is soft and pliable, makes kinking with complete occlusion possible. When this occurs in the expiratory pathway of an Ayre's T-piece system the gas flow is diverted into the lungs. The volume supplied will exceed the vital capacity of a 3-kg child in less than 3 seconds and barotrauma will occur soon afterwards unless precautions have been taken to prevent it.

One solution is to change the design of the headset; armoured or corrugated tubing is used in other situations where occlusion may be dangerous.[1] Protection by means of a pressure relief valve is vital when obstruction is possible.[2] Ideally this valve should be placed on the respiratory pathway as close to the gas supply as possible (Fig. 1, point D), in this position it will not interfere with the use of the system; it should blow off at a mouth pressure of less than 5.0 kPa,[3] but not at normal ventilatory pressures and should be reliable and widely available.

The Vickers 4.0 kPa valve fits these criteria. It opens at between 3.4 and 3.9 kPa at a variety of gas flows between 4 and 15 litres/minute. If the valve is put at the proximal end of the inspiratory tube there is a pressure drop between the valve and the mouth. This can be significant if the tubing is narrow or extremely long. We recommend that it should be no longer than 2 m and no less than 6 mm in diameter. The valve will open under these circumstances at mouth pressures of 3.3–3.5 kPa at gas flows of 4–10 litres/minute in the majority of cases. This allows adequate ventilation and the generation of vital capacity breaths for physiotherapy in most cases.

Royal Victoria Infirmary,
Newcastle upon Tyne NE1 4LP

G.D. Prince
B.J. Nicholls

References

1. Kubota Y, Toyoda Y, Kubota H, Ishida H. Armoured tubes are necessary for neuroanaesthesia. *Anaesthesia* 1986; **41:** 1064–5.
2. Newton NI, Adams AP. Excessive airway pressure during anaesthesia. Hazards, effects and prevention. *Anaesthesia* 1978; **33:** 689–99.
3. Rosen M, Laurence KM. Expansion pressures and rupture pressures in the newborn lung. *Lancet* 1965; **2:** 721–2.

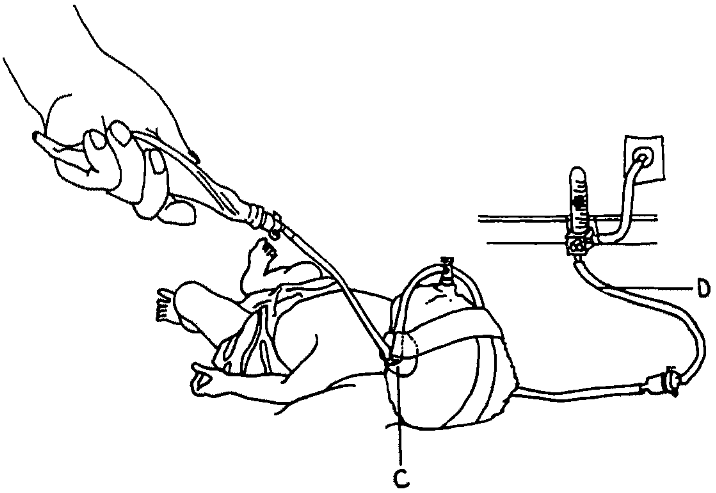


Fig. 1.

Anaesthesia for carbon dioxide laser laryngeal surgery in infants

The new Oswal–Hunton paediatric metal tracheal tube for laser surgery in infants (*Anaesthesia* 1988; **43:** 394–6) seems a very useful and welcome addition to our equipment. Unfortunately the name of the supplier was given but no address.* There are some reservations about its use in patients breathing spontaneously through a nasopharyngeal catheter: the relevant structures move with breathing; patient movement (contraindicated in laser surgery) is not impossible; the variability of infant respiratory response to the quoted halothane concentrations may include hypoventilation or even apnoea; the anaesthetist does not have total control of the airway and the need for constant vigilance seems an understatement. Moreover, the trauma of the actual surgery and the passage and manipulation of laryngoscopes and bronchoscopes on the larynx make what the anaesthetist does, by gentle introduction of a tracheal tube, pale into insignificance.

Recently a 1-year-old 7.4 kg child was presented for examination under anaesthesia, and possible laser surgery, of subglottis and right vocal cord haemangioma. The former procedure, which lasted 60 minutes, was performed under nitrous oxide–halothane (via nasotracheal tube) and oxygen–halothane (via ventilating bronchoscope). The latter procedure took 70 minutes. Anaesthesia for this phase was intermittent thiopentone and suxamethonium at first and then intermittent ketamine and suxamethonium. A suitable ENT coagulation/suction metal cannula was selected to act as a narrow diameter tracheal tube or jet (external diameter under 2 mm). This was introduced into the trachea and held against the inside of the operating laryngoscope, out of the field of the laser, by a surgeon. Carefully controlled and appropriately adjusted ventilation was applied, between periods of laser operation, by operation of the manual switch of the conventional pipeline oxygen venturi set-up. No problems were experienced in the operating room or recovery room and therefore adrenaline nebulisation or dexamethasone were not given. No further treatment was found necessary at a subsequent examination under anaesthesia some days later.

The surgery was performed using the Zeiss Opmilas CO_2-L Laser system through an operating microscope with micromanipulator control and the use of vocal cord retractors as necessary. It seems possible in this way to make the restriction of access to the posterior larynx and subglottis relative rather than absolute i.e. the position of the jet cannula can be varied, the operation field is highly magnified, and the very narrow laser beam is finely controlled.

The problems of access and airway control become more acute as infant size and age decrease. This case report describes one possible approach where the procedure is lengthy. Unlike Spargo and Neilsen (*Anaesthesia* 1989; **44:** 80–1) I hesitate to regard anything in anaesthesia as simple since this attitude can be the first step on the path to a mishap. The ability and adaptability of the anaesthetist cannot be overemphasised in this field.

University of Natal,
Box 17039,
Congella 4013
South Africa

R. Williamson

The ethics of difficult tracheal intubation

Concern for the patient involved prompts expression of my opinion that the suggestion by Dr Callender,[1,2] of elective tracheostomy performed under local anaesthesia at 34 weeks' gestation of any pregnancy in the 30-year-old patient described, is unacceptable.

Several years ago an identical problem occurred here. A nursing sister required laparoscopy and tubal surgery but a consultant anaesthetist was unable to intubate. Because general anaesthesia had been used at this attempt I knew her not to have a difficult airway and gave a thiopentone–suxamethonium induction, found her to be a Grade IV laryngoscopy,[3] and performed a simple straightforward blind nasal intubation. She subsequently became pregnant.

The thought of a tracheostomy did not enter anyone's mind and I am certain that the patient would have been aghast at the suggestion. She ensured, on admission to hospital, that all her doctors knew about her experiences and my involvement in her intubation, so that contact could be made if necessary. This she will do whenever general anaesthesia is required in the future. Delivery was by elective Caesarian section under epidural anaesthesia conducted by a consultant anaesthetist. However, if I had to be called without notice, or to be on 24-hour call or even in the hospital on 24-hour availability to assist this or any other patient for such a problem, it would be done. Specialists in paediatric, obstetric, vascular, cardiac, neurosurgical anaesthesia do this, so why not for intubation? Surely an advanced and sophisticated centre in the United Kingdom can provide this cover?

Ethically, in the case described by Dr Callender, one can question a number of points. On two previous occasions surgery was abandoned because of failure to pass a tube. There was thus ample opportunity to ensure the presence of someone who possessed intubation expertise when she presented for tubal surgery or, alternatively, for her referral to a centre where such expertise was available. The persistence at attempts to intubate, for elective surgery, for such an excessive period of time seems unnecessary. Such 'personitis' or reluctance to delegate or refer is well recognised in the causation of accidents.[4] In my experience the quoted duration needed to achieve intubation, or any other practical manoeuvres performed by doctors, is no good indicator of how long someone else might take which could possibly be only a matter of seconds. Certainly expertise and experience are important but commonly the delay can be due to slowness in doing the correct thing which also derives from relative lack of the former two. Finally, there is the infliction of prolonged physical, psychological and cosmetic trauma, and risk, which is to my mind unnecessary, unavoidable, and impossible to justify.

University of Natal,
Box 17039,
Congella 4013,
South Africa

R. Williamson

**Editor's note.* Dr Hunton informs us that the tubes in question are distributed by Messrs J.B. Masters, Red Marsh Drive, Redmarsh Industrial Estate, Thornton Cleveleys, Lancashire, and, Leyland Medical, P.O. Box 6, Tuer Street, Leyland, Preston PR5 LXR.

References

1. Callander CC, Thomas JS. The ethics of difficult tracheal intubation. *Anaesthesia* 1988; **43:** 703–4.
2. Callander CC. 'Ethics' of difficult intubation. *Anaesthesia* 1989; **44:** 269.
3. Cormack RS, Lehane J. Difficult tracheal intubation in obstetrics. *Anaesthesia* 1984; **39:** 1105–11.
4. Allnutt MF. Human factors in accidents. *British Journal of Anaesthesia* 1987; **59:** 856–64.

Anaesthetists as physicians

The editorial by Dr Jones (*Anaesthesia* 1989; **44:** 377–8) was interesting, however, I disagree with him on one point. He suggests that when an anaesthetist plays a part in planning the optimum timing of surgery he is displaying 'physicianship'. Physicians are very worthy people but they do not have a monopoly on sensible decision making. When an anaesthetist assesses a patient and uses the information to help plan treatment he is simply acting as a competent anaesthetist; there is no need to invoke the presumed qualities of any other specialty.

Princess Margaret Hospital,
Swindon SN1 4JU
M. O'Connor

A reply

'*Physician*'[1]: one who practises the healing art including medicine and surgery; one legally qualified in both medicine and surgery; specialist in medicine and surgery; specialist in medical diagnosis and treatment; healer.[1]

I am sorry that Dr O'Connor feels that anaesthetists cannot include themselves in this definition.

Guys Hospital,
London SE1 9RT
R.M. Jones

Reference

1. Sykes JB, ed. *The concise Oxford dictionary*, 7th edn. Oxford: Oxford University Press, 1982: 772.

Bad publicity

It was naturally of concern to me to read the letter from Dr P.M.H. de Boulay (*Anaesthesia* 1989; **44:** 70) which referred to an article which appeared in the *Sunday Telegraph* in July, 1988. An enquiry was made by the Faculty of Anaesthetists as a result of this publication about the content of the report and its potential effect on trainees. I am happy to inform you that the Faculty were completely satisfied that the item misrepresented my own clinical practice and was an inaccurate account of anaesthesia at Charing Cross Hospital.

It would appear that journalists involved with this type of news item are more concerned with sensationalism rather than with accuracy. Had I prior knowledge of either the standard of the *Sunday Telegraph* reporting, or that the resultant misrepresentations would be unamendable, I should naturally have been far less prepared to associate with the journalists concerned.

Charing Cross Hospital,
Fulham Palace Road,
London W6 8RF
J. Stevens

Anaesthesia, 1989, Volume 44, pages 795–796

Book reviews

Respiratory physiology—an analytical approach 795
Edited by H.K. Chang and M. Paiva
Surgery for anaesthetists 795
Edited by J.S.M. Zorab
Fluids, electrolytes and acid bases 796
Edited by G. Tom Shires
Pocket manual of anesthesia 796
G. Lenz, B. Kottler, R. Schorer and W.E. Spoerel
Fourth report of the Victorian consultative council on anaesthetic mortality and morbidity—cases reported during 1986 796
Edited by J.D. Paul and G.D. Robinson
On chloroform and other anaesthetics 796
John Snow
Books received 796

Respiratory physiology—an analytical approach

Edited by H.K. Chang and M. Paiva. Pp. xv + 869. Marcel Dekker, 1989. $150.00 USA and Canada; $180.00 all other countries.

This book is part of a series which has over the years contained several issues of practical interest and value to anaesthetists, such as acute respiratory failure, chronic obstructive lung disease, and high frequency ventilation. This volume is of less immediate relevance, and readers of *Anaesthesia* are likely to be either terrified or fascinated by it. One of the authors is Professor of Interdisciplinary Research and most of the contributors are either respiratory physicians, physiologists, or biomedical engineers who have used the ability to analyse the respiratory system mathematically, and to develop mathematical or physical models, to increase our understanding of how the lung works. If the reader were to be daunted by three-dimensional graphs, differential equations, and electrical analogues, then this book should be left alone. However, a lot of our understanding of anaesthetics is based on models, either mathematical or physical. Most anaesthetists know of fast and slow compartments, models of anaesthetic uptake, gas stores, breathing systems, and the shunt/ideal/deadspace model of pulmonary gas exchange. There is therefore no great step for them to approaching the models of the airways, the pulmonary vessels, or the interstitial space of the lung, that are described in this book. If the system can be described, and then modelled, prediction and understanding of disturbances will follow.

Some of the models are less accessible to intuitive reasoning: self-consistency recursions and Monte Carlo approximations leave this reviewer at the starting line. However, the book is generally a fascinating compendium of accounts of analytical physiology, covering a large range of topics although it is far from exhaustive. It covers morphometry, airway behaviour, gas mixing, ventilation distribution, mechanics of lung tissue, haemodynamics, fluid exchange and there is a final short chapter on models of respiratory control. Similar accounts of many of these topics can be found elsewhere, but their collection into a single volume results in a remarkable book, but one that may not be to everyone's taste. The standard of production is high: the book is well printed on good paper, and well bound. The illustrations are generally good and in some cases, particularly the micro-anatomical illustrations of Horsfield and Weibel, they are superb. The text is well laid out and there are remarkably few errors. The index is short and barely adequate, however. For those who are interested in the formal approach to physiology, or in respiratory physiology (which depends largely on this type of approach) this book will be a joy only offset by the high price, which is an unfortunate feature of this series.

G.B. Drummond

Surgery for anaesthetists

Edited by J.S.M. Zorab. Pp. xiii + 512. Blackwell Scientific, 1988. £65.50.

The anaesthetist today has to work alongside surgeons of all specialties who perform an ever increasing number of diverse, complex, and often very lengthy procedures. This book was clearly aimed at this problem and states at the outset that 'the surgical teaching is orientated towards the needs of the anaesthetic trainees'. With this in mind, the editor has gathered contributions from 20 surgeons and 14 anaesthetists and produced a well written and profusely illustrated text.

There is a useful initial chapter on electrical hazards in the operating room and the book is then subdivided into the major surgical specialties. Each chapter has combined contributions from at least one surgeon and one anaesthetist and this should have produced a well-balanced review to achieve the stated aims. In some chapters, notably those on hepatic surgery, surgery of oesophageal varices and endocrine procedures, this is the case and there are clearly points of direct relevance to anaesthetists, but on the whole the book falls short of its objective. The text contains too much detail about surgical diagnosis, for example urodynamics, indications for operations and long-term postoperative complications such as vitamin deficiencies. Elsewhere the authors discuss important issues such as the limitation of anaesthetic access by major incisions in plastic surgery and surgery for burns, but cloud these points by adopting the same approach to hernia repair and appendicectomy.

Overall the text represents an up-to-date overview by a distinguished multi-author panel but fails to surpass many of the basic volumes of surgery already available. The reader is left with the feeling that some integrating part of the text has been omitted from the end of each chapter (usefully a summary), and a more appropriate title would probably have been 'A synopsis of surgery with useful hints for anaesthetists'. The combination of this and the book's size and price (hardback) are likely to deter most of the intended readership.

A. Dennison
(Senior Lecturer, Surgery)

Fluids, electrolytes and acid bases

Edited by G. Tom Shires, Pp. x + 203. Churchill Livingstone, 1988. £27.50.

This book is the 15th in the series of *Clinics in critical care medicine*. It is written exclusively by American surgeons. General principles of fluid and electrolyte balance are discussed concisely by the editor and three chapters are devoted to acid-base balance, with an emphasis on the responses to injury and haemorrhage. These first four chapters are good, but routine.

The remainder of the book is devoted to discussion of diagnosis and management of fluid and acid-base disorders associated with specific abnormalities. The relationship between chemical mediators and fluid and electrolyte movement across the cell membrane is discussed in depth. Two chapters are devoted to consideration of haemorrhagic shock. The emphasis of the first is on fluid shifts and therapy; the second concentrates on the endocrine response. Fluid replacement regimens used in the management of patients with burns are described in a very readable and practical chapter. Cardiogenic shock and sepsis are discussed and nutritional requirements after trauma or surgery are evaluated.

This is not the best book in the series. One of the reasons, I think, is that a volume of half the size could have dealt with the topic satisfactorily. Because of its length, authors have either covered the same ground, which has resulted in a considerable degree of overlap, or strayed completely off the subject of fluids, electrolytes and acid-base balance. For example, the chapter on sepsis does not mention these topics at all and 75% of the text is used to discuss the correct choice of antibiotics in the surgical patient. Similarly, the description of cardiogenic shock excludes all discussion of fluids or pH, other than to mention that volume replacement should be administered cautiously. Little consideration is given to the requirements of the nonsurgical patient and the effect of fluid and electrolyte shifts on pulmonary function is almost ignored. There is a very clear bias throughout the book against the use of colloid solutions; this may or may not be justified, but the contributors should have been permitted to present both sides of the argument.

Many books in this series have been valuable assets in the anaesthetic department, operating theatre and intensive care unit. This volume contains useful information, but it is diluted by discussion of topics which are described elsewhere in much more detail and with greater style. Surgeons may find it useful, but the British intensive care specialist will learn little that is new.

A.R. Aitkenhead

Pocket manual of anesthesia

G. Lenz, B. Kottler, R. Schorer and W.E. Spoerel. Pp. xi + 318. B.C. Decker, 1988. £14.50.

This is the decade of pocket manuals, those treasure troves of useful facts, that fit snugly into the pocket of a white coat and provide authoritative information in every crisis. Their continued appearance testifies to the popularity of the aim but the difficulty of finding the right format. This manual does at least actually fit in a pocket! Unfortunately, it reads as it is, a mid-Atlantic translation of a German text.

The 23 chapters start with premedication, pass on to the working environment and technical aspects of anaesthesia, and then to solutions and drugs that are commonly used. There are then chapters on regional anaesthesia, paediatric anaesthesia and resuscitation, ending up with the special situations, a long miscellany of just those problems one might hope to be supported through by some specific critical information from a *vade mecum*.

Alas this book fails. The information given is very uneven: the chapter on plasma substitutes mentions only dextrans and albumin solutions. Is it worth discussing brachial plexus block without even a mention of the supraclavicular approach? Drug names have not been changed for the British reader, nor has the selection of drugs discussed; few will be grateful for two pages on propafenon. Considering difficult intubation, this reviewer was not enlightened to find listed in fourth position Strumpell–Marie–Bekhterev's disease (in fact, ankylosing spondylitis!).

But the most important feature of any such manual must be its index. This must have been created by a key-word searching computer. How else could 'postoperative pain' take one into the myasthenia gravis section, a page which admittedly contains a passing reference to postoperative pain. Seeking a discussion of intubation problems, 'intubation' takes one into causes for raised intracranial pressure.

Such a compilation clearly represents a massive effort by its authors but the book has not travelled well and needs to be rewritten before it is likely to prove a useful addition to the literature. It cannot be recommended in its present form to the British anaesthetist.

M. Lindop

Fourth report of the Victorian consultative council on anaesthetic mortality and morbidity—cases reported during 1986

This report, edited by J.D. Paul and G.D. Robinson, is available from the Health Department, 555 Collins Street, Melbourne, Australia 3001. It contains descriptions of 36 cases of patients who died at some unspecified interval during or after an operation and 63 critical incidents or cases of serious morbidity.

J.N. Lunn

On chloroform and other anaesthetics

John Snow, third facsimile edition, published by Wood Library-Museum, 515 Busse Highway, Park Ridge, Illinois 60068, USA.

This classic book is, according to the new Foreword by N.M. Greene, still in demand and may be obtained from the publishers at a price of US$41; payment in that currency please.

J.N. Lunn

Books received

We thank the publishers for the following books, some of which may be reviewed in future issues of the journal.

Clinical application of blood gases, 4th edn
B.A. Shapiro, R.A. Harrison, R.D. Cane and R. Templin. Pp. xvi + 379. Year Book Medical, 1989. £21.50.

Talking health: conventional and complementary approaches
Edited by J. Watt and C. Wood. Pp. 167. Royal Society of Medicine, 1989. £4.95.

Anaesthesia and malignant disease
J. Filshie and D.S. Robbie. Pp. xv + 303. Edward Arnold, 1989. £27.50.

Perspectives and shock research—metabolism, immunology, mediators, and models
Edited by J.C. Passmore. Pp. xvii + 346. Alan R. Liss, 1989. $70.00.

Anaesthesia, 1989, Volume 44, pages 797–802

Anaesthetic literature

This section of *Anaesthetic literature* contains references taken from *Current Contents—Life Sciences* for May 1989. The Journals which may be consulted when *Anaesthetic literature* is compiled are those listed in *Current Contents—Life Sciences*, published by the Institute of Scientific Information, Philadelphia, Pennsylvania, USA.

Abdominal surgery

Hormonal control of gastric and colorectal cancer in man. Morris DL, Watson SA *et al. Gut* 1989; **30:** 425.

Oxygen radicals—mediators of gastrointestinal pathophysiology. Parks DA. *Gut* 1989; **30:** 293.

Pharmacology

Adrenergic drugs and their antagonists

Aqueous humor concentration of metoprolol after oral administration. Calissendorff B, Savvaides I. *Journal of Ocular Pharmacology* 1989; **5:** 27.

Effect of salbutamol on digoxin concentration in serum and skeletal muscle. Edner M, Jogestrand T. *European Journal of Clinical Pharmacology* 1989; **36:** 235.

Beta-adrenoceptor responses to inhaled salbutamol in normal subjects. Lipworth BJ, McDevitt DG. *European Journal of Clinical Pharmacology* 1989; **36:** 239.

Molecular biology of adrenergic and muscarinic cholinergic receptors. A perspective. Venter JC, Fraser CM *et al. Biochemical Pharmacology* 1989; **38:** 1197.

Anaesthetic agents

The pharmacokinetics of volatile anesthetic agent elimination: a theoretical study. Bailey JM. *Journal of Pharmacokinetics and Biopharmaceutics* 1989; **17:** 109.

Respiratory center output following zopiclone or diazepam administration in patients with pulmonary disease. Beaupre A, Soucy R *et al. Respiration* 1988; **54:** 235.

Importance of genetic factors in the regulation of diazepam metabolism: relationship to S-mephenytoin, but not debrisoquin, hydroxylation phenotype. Bertilsson L, Hentborn TK *et al. Clinical Pharmacology and Therapeutics* 1989; **45:** 348.

Pharmacokinetic and electroencephalographic study of intravenous diazepam, midazolam and placebo. Greenblatt DJ, Ebrenberg BL *et al. Clinical Pharmacology and Therapeutics* 1989; **45:** 356.

Intersubject variation in the pharmacokinetics of haloperidol and reduced haloperidol. Midha KK, Chakraborty BS *et al. Journal of Clinical Psychopharmacology* 1989; **9:** 98.

Effects of diazepam and flumazenil on sedation and hypoxic ventilatory response. Mora CT, Torjman M, White PF. *Anesthesia and Analgesia* 1989; **68:** 473.

Steroid anesthetics and naturally occurring analogs moderate the gamma-aminobutyric acid receptor complex at a site distinct from barbiturates. Turner DM, Ransom RW *et al. Journal of Pharmacology and Experimental Therapeutics* 1989; **248:** 960.

Benzodiazepine antagonism does not provoke a stress response. White PF, Shafer A *et al. Anesthesiology* 1989; **70:** 636.

Analgesic agents

Evaluation of adenosine agonists as potential analgesics. Davis KH, Chippari S *et al. European Journal of Pharmacology* 1989; **162:** 365.

Long lasting respiratory depression induced by morphine-6-glucuronide? Hasselstrom J, Berg U *et al. British Journal of Clinical Pharmacology* 1989; **27:** 515.

The bioavailability and pharmacokinetics of morphine after intravenous, oral and buccal administration in healthy volunteers. Hoskin PJ, Hanks GW *et al. British Journal of Clinical Pharmacology* 1989; **27:** 499.

Naloxone suppresses buprenorphine stimulation of plasma prolactin. Mendelson JH, Mello NK *et al. Journal of Clinical Psychopharmacology* 1989; **9:** 105.

Antagonist effects of nalbuphine in opioid-dependent human volunteers. Preston KL, Bigelow GE, Liebson IA. *Journal of Pharmacology and Experimental Therapeutics* 1989; **248:** 929.

Analgesic use and chronic renal disease. Sandler DP, Smith JC *et al. New England Journal of Medicine* 1989; **320:** 1238.

Effect of morphine on cortisol and prolactin secretion in anorexia nervosa and depression. Zis AP, Remick RA *et al. Clinical Endocrinology* 1989; **30:** 421.

Muscle relaxants

Plasma cholinesterase activity in patients during therapy with dexamethasone or prednisone. Bradamante V, Kunecvajic E *et al. European Journal of Clinical Pharmacology* 1989; **36:** 253.

Effects of droperidol, haloperidol and ketamine on halothane, succinylcholine and caffeine contractures—implications for malignant hyperthermia. Fletcher JE, Rosenberg H, Lizzo FH. ACTA ANAESTHESIOLOGICA SCANDINAVICA 1989; **33:** 187.

Antagonism by tubocurarine and verapamil of the regenerative acetylcholine release from mouse motor nerve. Hong SJ, Chang CC. EUROPEAN JOURNAL OF PHARMACOLOGY 1989; **162:** 11.

Seasonal variation in blood cholinesterase activity. Ratner D, Barsella P *et al. Israel Journal of Medical Sciences* 1989; **25:** 247.

Myasthenic syndrome caused by direct action of chloroquine on neuromuscular junction. Robberecht W, Bednank J *et al. Archives of Neurology* 1989; **46:** 464.

Other drugs

Cytochrome P-450 metabolism of arachidonic acid—formation and biological actions of epoxygenase-derived eicosanoids. Fitzpatrick FA, Murphy RC. *Pharmacological Reviews* 1988; **40:** 229.

Cimetidine-nicoumalone interaction in man: stereochemical considerations. Gill TS, Hopkins KJ *et al. British Journal of Clinical Pharmacology* 1989; **27:** 469.

The molecular biology of cytochrome P-450s. Gonzalez FJ. *Pharmacological Reviews* 1988; **40:** 243.

The collator of this section is Dr L. Kaufman, MD, FFARCS, 145 Harley Street, London W1N 2DE. Dr Kaufman is prepared to provide on request, and at a modest charge, a new additional service to our readers. References from January 1984 have been entered on data base. The data are held on Dbase II, cpm 86 and on Dbase II, MsDos and are available on disc, together with a program providing search facilities. Enquiries direct to Dr Kaufman at the above address please.

Influence of vitamin B6 status on aspects of lead poisoning in rats. McGowan C. *Toxicology Letters* 1989; **47:** 87.

Bioavailability/bioequivalence—study design and statistical issues. Metzier CM. *Journal of Clinical Pharmacology* 1989; **29:** 289.

The hemodynamic effects of intravenous ranitidine in intensive care unit patients—a double-blind prospective study. Onofrey O, Kelly KM *et al.* Journal of Clinical Pharmacology 1988; **28:** 1098.

Treatment of gram-negative infections in patients with renal impairment—new alternatives to aminoglycosides. Whelton A. *Journal of Clinical Pharmacology* 1988; **28:** 866.

Apparatus

Central venous catheter vascular erosions: diagnosis and clinical course. Ellis LM, Vogel SB, Copeland EM III. *Annals of Surgery* 1989; **209:** 475.

Low frequency oscillatory ventilation through the suction channel of a pediatric bronchoscope. Nutman J, Waldemar A *et al. Annals of Otology, Rhinology and Laryngology* 1989; **98:** 251.

Editorial: a new approach to measurement of lung mechanics. Park SS. *Lung* 1989; **167:** 137.

The high price of 'sleep': can Australia afford high-technology anaesthesia? Riley R. *Medical Journal of Australia* 1989; **150:** 454.

Pulse oximetry. Tremper KK. *Chest* 1989; **95:** 713.

Complications

Prevention of intraoperative anesthesia accidents and related severe injury through safety monitoring. Eichhorn JH. *Anesthesiology* 1989; **70:** 572.

Rubber anaphylaxis. Slater JE. *New England Journal of Medicine* 1989; **320:** 1126.

General anaesthetic procedures

Deep vein thrombosis after total hip replacement—a comparison between spinal and general anaesthesia. Davis FM, Laurenson VG *et al. Journal of Bone and Joint Surgery* 1989; **71:** 181.

Attenuation of the pressor response to laryngoscopy and tracheal intubation with intravenous verapamil. Nishikawa T, Namiki A. *Acta Anaesthesiologica Scandinavica* 1989; **33:** 232.

Alfentanil obtunds the cardiovascular and sympathoadrenal responses to suxamethonium-facilitated laryngoscopy and intubation. Scheinin B, Scheinin M *et al. British Journal of Anaesthesia* 1989; **62:** 385.

General interest

Tracheostomies in burn patients. Jones WG, Madden M *et al. Annals of Surgery* 1989; **209:** 471.

Spinal and epidural analgesia

Epidural anesthesia in patients undergoing thoracic surgery. Temeck BK, Schafer PK *et al. Archives of Surgery* 1989; **124:** 415.

Spinal opioids

Respiratory depression and spinal opioids. Etches RC, Sandler AN, Daley MD. *Canadian Journal of Anaesthesia* 1989; **36:** 165.

Localization of dynorphin-induced neurotoxicity in rat spinal cord. Stewart P, Isaac L. *Life Science* 1989; **44:** 1505.

Minimal effective dose of intrathecal morphine for pain relief following transabdominal hysterectomy. Yamaguchi H, Walanabe S *et al. Anesthesia and Analgesia* 1989; **68:** 537.

Obstetric anaesthesia and analgesia

Diabetes and pregnancy. Barss VA. *Medical Clinics of North America* 1989; **73:** 685.

Influence of preoperative gastric aspiration on the volume and pH of gastric contents in obstetric patients undergoing caesarean section. Brockutne JG, Rout C *et al. British Journal of Anaesthesia* 1989; **62:** 397.

Spinal buprenorphine for postoperative analgesia after caesarean section. Celleno D, Capogna G. *Acta Anaesthesiologica Scandinavica* 1989; **33:** 236.

Effects of subacute opioid administration in the rat on the initiation, duration and outcome of parturition and maternal levels of oxytocin and AVP. Evans RG, Olley JE *et al. Clinical and Experimental Pharmacology and Physiology* 1989; **16:** 169.

Acute coagulopathy in pregnancy. Finley BE. *Medical Clinics in North America* 1989; **73:** 723.

Cardiac disease in pregnancy. Gianopoulos JG. *Medical Clinics of North America* 1989; **73:** 639.

Anticoagulants during pregnancy. Ginsberg JS, Hirsh J. *Annual Review of Medicine* 1989; **40:** 79.

Pregnancy in organ transplant recipients. Hou S. *Medical Clinics of North America* 1989; **73:** 667.

Valproic acid disposition and protein binding in pregnancy. Koerner M, Yerby M *et al. Therapeutic Drug Monitoring* 1989; **11:** 228.

Hypertensive disorders of pregnancy. Leading Article. *Lancet* 1989; **1:** 935.

Preeclampsia: pathophysiology, diagnosis, and management. Lindheimer MD, Katz AI. *Annual Review of Medicine* 1989; **40:** 233.

Pulmonary edema associated with tocolytic therapy. Pisani RJ, Rosenow EC III. *Annals of Internal Medicine* 1989; **110:** 714.

The effect of epidural sufentanil on shivering and body temperature in the parturient. Sevarino FB, Johnson MD *et al. Anesthesia and Analgesia* 1989; **68:** 530.

Arterial to end-tidal carbon dioxide tension difference during anaesthesia in early pregnancy. Shanker KB, Moseley H *et al. Canadian Journal of Anaesthesia* 1989; **36:** 124.

Source of increased plasminogen activators during pregnancy and puerperium. Shimada H, Takashima E *et al. Thrombosis Research* 1989; **54:** 91.

Acute hypertensive crisis in pregnancy. Silver HM. *Medical Clinics of North America* 1989; **73:** 623.

A comparison of morphine, meperidine, and oxymorphone as utilized in patient-controlled analgesia following cesarean delivery. Sinatra RS, Lodge K *et al. Anesthesiology* 1989; **70:** 585.

Pharmacologic management of acute mania in pregnancy. Sitland-Marken PA, Rickman LA *et al. Journal of Clinical Psychopharmacology* 1989; **9:** 78.

Paediatric anaesthesia and intensive care

Necrotising tracheobronchitis following mechanical ventilation of the newborn. Arad I, Uwyyed K *et al. Israel Journal of Medical Sciences* 1989; **25:** 271.

Prognosis of newborn infants with hypoxic-ischemic brain injury assessed by phosphorus magnetic resonance spectroscopy. Azzopardi D, Wyatt JS *et al. Pediatric Research* 1989; **25:** 445.

Pulmonary oedema after acute asphyxia in a child. Boykett M. *British Medical Journal* 1989; **298:** 928.

Atrial natriuretic factor during the perinatal period: equal depletion in both atria. Dolan LM, Young CA *et al. Pediatric Research* 1989; **25:** 339.

Mechanical ventilation for status asthmaticus in children. Dworkin G, Kattan M. *Journal of Pediatrics* 1989; **114:** 545.

Effects of reductions in hemoglobin-oxygen affinity and hematocrit level on oxygen consumption and acid-base state in fetal lambs. Edelstone DI, Darby MJ *et al. American Journal of Obstetrics and Gynecology* 1989; **160:** 820.

Risks to the fetus of anticoagulant therapy during pregnancy. Ginsberg JS, Hirsh J *et al. Thrombosis and Haemostasis* 1989; **61:** 197.

Carbon dioxide elimination in anaesthetized children. Lindahl SGE, Offord KP *et al. Canadian Journal of Anaesthesia* 1989; **36:** 113.

Fetal vascular responses to prostacyclin. Parisi VM, Walsh SW. *American Journal of Obstetrics and Gynecology* 1989; **160:** 871.

A comparison of the rheologic properties of neonatal and adult blood. Rampling MW, Whittingstall P *et al. Pediatric Research* 1989; **25:** 457.

Lorazepam pharmacodynamics and pharmacokinetics in children. Relling MV, Mulhern RK *et al. Journal of Pediatrics* 1989; **114:** 641.

Effects of negative upper airway pressure on pattern of breathing in sleeping infants. Thach BT, Menon AP, Scheft GL. *Journal of Applied Physiology* 1989; **66:** 1599.

Cardiovascular system

Physiology

Effect of captopril (an angiotensin-converting enzyme inhibitor) on intraocular pressure in healthy human volunteers. Al-Sereiti MR, Turner P. *Journal of Ocular Pharmacology* 1989; **5:** 1.

A theoretical view of interstitial fluid pressure-volume measurements. Blake TR. *Microvascular Research* 1989; **37:** 178.

Cardiac norepinephrine kinetics in hypertrophic cardiomyopathy. Brush JE, Eisenhofer G *et al. Circulation* 1989; **79:** 836.

The effect of age on cerebral blood flow during hypothermic cardiopulmonary bypass. Brusino FG, Reves JG *et al. Journal of Thoracic and Cardiovascular Surgery* 1989; **97:** 541.

The human pressor response during and following voluntary and evoked isometric contraction with occluded local blood supply. Bull RK, Davies CTM *et al. Journal of Physiology* 1989; **411:** 63.

The contribution of atrial systole to mitral diastolic blood flow increases during exercise in human. Channer KS, Jones JV. *Journal of Physiology* 1989; **411:** 53.

Chronic and acute volume expansion in normal man: effect on atrial diameter and plasma atrial natriuretic peptide. Cuneo RC, Espiner EA *et al. Hormone and Metabolic Research* 1989; **21:** 148.

Review: Erythropoietin in health and disease. Eckardt KU, Bauer C. *European Journal of Clinical Investigation* 1989; **19:** 117.

Cardiorenal effects of atrial naturiuretic factor administration in congestive heart failure: natriuresis and diuresis without hemodynamic alterations. Firth BG, Pema R *et al. American Journal of the Medical Sciences* 1989; **297:** 203.

Lung is an important source of atrial natriuretic factor in experimental cardiomyopathy. Gutkowska J, Nemer M *et al. Journal of Clinical Investigation* 1989; **83:** 1500.

Effective hepatic blood flow during cardiopulmonary bypass. Hampton WW, Townsend MC *et al. Archives of Surgery* 1989; **124:** 458.

Heart rate response to breath-hold, valsalva and Mueller maneuvers in obstructive sleep apnea. Hanly PJ, George CF *et al. Chest* 1989; **95:** 735.

Natural killer cells as regulators of hematopoiesis. Hansson M, Petersson M *et al.* In: Ades EW, Lopez C, eds. *Natural killer cells and host defense*. Basel: S. Karger AG, 1989: 50.

Pharmacological modification of O_2 affinity improves deformability of deoxygenated sickle erythrocytes: possible therapy to sickle cell disease. Keidan AJ, Sowter MC *et al. Clinical Science* 1989; **76:** 357.

Increased blood pressure during potassium depletion in normotensive men. Krishna GG, Miller E, Kapoor S. *New England Journal of Medicine* 1989; **320:** 1177.

Cyclic GMP and mechanisms of vasodilation. Lincoln TM. *Pharmacology and Therapeutics* 1989; **41:** 479.

Plasma atrial natriuretic peptide in carcinoid heart disease. Lundin L, Oberg K *et al. American Journal of Cardiology* 1989; **63:** 969.

Peptide regulatory factors. Haemopoietic factors. Metcalf D. *Lancet* 1989; **1:** 825.

Circadian variation and triggers of onset of acute cardiovascular disease. Muller JE, Tofler GH, Stone PH. *Circulation* 1989; **79:** 733.

Age-dependency of left ventricular filling dynamics and relaxation as assessed by pulsed doppler echocardiography. Myreng Y, Nitter-Hauge S. *Clinical Physiology* 1989; **9:** 99.

The biochemical pharmacology of atrial peptides. Needleman P, Blaine EH *et al. Annual Review of Pharmacology and Toxicology* 1989; **29:** 23.

Prognostic significance of a low peak serum creatinine kinase level in acute myocardial infarction. Pierard LA, Dubois C *et al. American Journal of Cardiology* 1989; **63:** 792.

Renal interaction of atrial natriuretic peptide with angiotensin II: glomerular and tubular effects. Rakugi H, Ogihara T *et al. Clinical and Experimental Pharmacology and Physiology* 1989; **16:** 97.

Blood pressure and vasoactive hormones with improved glycaemic control in patients with diabetes mellitus. Richards AM, Donnelly T *et al. Clinical and Experimental Hypertension* 1989; **11:** 391.

Non-insulin dependent diabetes and ischaemic heart disease. Salonen JT. *British Medical Journal* 1989; **298:** 1050.

Effect of the venodilated state on sympathetic-induced venoconstriction in normal subjects. Sumner A, Zelis R *et al. American Journal of Cardiology* 1989; **63:** 973.

The relative antithrombotic effectiveness of heparin, a low molecular weight heparin, and a pentasaccharide fragment in an animal model. Thomas DP, Merton RE *et al. Thrombosis and Haemostasis* 1989; **61:** 204.

Increased circulating concentration of atrial natriuretic factor in persons with pheochromocytomas. Vesely DL, Arnold WC *et al. Clinical and Experimental Hypertension* 1989; **11:** 353.

Treatment and medication

Respiratory effects of angiotensin converting enzyme inhibition. Berkin KE. *European Respiratory Journal* 1989; **2:** 198.

Protective effect of the specific thromboxane receptor antagonist, BM-13505, in reperfusion injury following acute myocardial ischemia in cats. Bhat AM, Sacks H *et al. American Heart Journal* 1989; **117:** 799.

Comparison of trauma assessment scores and their use in prediction of infection and death. Cheadle WG, Wilson M *et al. Annals of Surgery* 1989; **209:** 541.

Usefulness of propafenone for recurrent paroxysmal atrial fibrillation. Connolly SJ, Hoffert DL. *American Journal of Cardiology* 1989; **63:** 817.

A comparison of the hypotensive effects of captopril and atenolol in the treatment of hypertension in diabetic patients. Elving LD, Denobel E *et al. Journal of Clinical Pharmacology* 1989; **29:** 316.

Antitachycardia pacing and implantable cardioverter defibrillators. Furman S, Mercando AD. *Annual Review of Medicine* 1989; **40:** 123.

Limitations to donating adequate autologous blood prior to elective orthopedic surgery. Goodnough LT, Wasman J *et al. Archives of Surgery* 1989; **124:** 494.

Adverse hemodynamic and clinical effects of encainide in severe chronic heart failure. Gottlieb SS, Kukin ML *et al. Annals of Internal Medicine* 1989; **110:** 505.

Plasma levels of atrial natriuretic peptide during myocardial ischemia induced by percutaneous transluminal coronary angioplasty or dynamic exercise. Ikaheimo MJ, Ruskaaho HJ *et al. American Heart Journal* 1989; **117:** 837.

Amiodarone hepatotoxicity: prevalence and clinicopathologic correlations among 104 patients. Lewis JH, Ranard RC *et al. Hepatology* 1989; **9:** 679.

Treatment of the elderly hypertensive patient with indenolol: a review. Malacco E, Gnemmi AE *et al. Current Therapeutic Research* 1989; **45:** 643.

Effect of sodium nitroprusside on spinal cord perfusion and paraplegia during aortic cross-clamping. Marini CP, Grubbs PE *et al. Annals of Thoracic Surgery* 1989; **47:** 379.

Identification of high-risk and low-risk subgroups of patients with mitral valve prolapse. Marks AR, Choong CY *et al. New England Journal of Medicine* 1989; **320:** 1031.

Effect of perioperative blood transfusion on outcome in patients with surgically resected lung cancer. Moores DWO, Piantadosi S, McKneally M. *Annals of Thoracic Surgery* 1989; **47:** 346.

Epinephrine-induced reversal of verapamil's electrophysiologic and therapeutic effects in patients with paroxysmal supraventricular tachycardia. Morady F, Kou WH *et al. Circulation* 1989; **79:** 783.

Intraoperative blood loss and patient and graft survival in orthotopic liver transplantation: their relationship to clinical and laboratory data. Motschman TL, Taswell HF *et al. Mayo Clinic Proceedings* 1989; **64:** 346.

Esmolol versus verapamil in the acute treatment of atrial fibrillation or atrial flutter. Platia EV, Michelson EL *et al. American Journal of Cardiology* 1989; **63:** 925.

Care of the patient after coronary angioplasty. Popma JJ, Dehmer GJ. *Annals of Internal Medicine* 1989; **110:** 547.

Clinical pharmacokinetic considerations in the control of oral anticoagulant therapy. Shetty HGM, Fennerty AG, Routledge P. *Clinical Pharmacokinetics* 1989; **16:** 238.

Effects of intravenous metoprolol on global and regional left ventricular function after coronary arterial reperfusion in acute myocardial infarction. Steingart RM, Matthews R *et al. American Journal of Cardiology* 1989; **63:** 767.

High dose nalbuphine in early acute myocardial infarction. Trouton TG, Adgey AAJ. *International Journal of Cardiology* 1989; **2:** 53.

Pulmonary vascular resistance before and after cardiopulmonary bypass—the effect of $Paco_2$. Viitanen A, Salmenpera M *et al. Chest* 1989; **95:** 773.

Intraoperative autologous transfusion: its role in orthotopic liver transplantation. Williamson KR, Taswell HF *et al. Mayo Clinic Proceedings* 1989; **64:** 340.

The effect of bunazosin, a new alpha l-blocker, on plasma lipids in diabetic subjects with essential hypertension. Yoshino G, Kazumi T *et al. Current Therapeutic Research* 1989; **45:** 677.

Incidence and clinical relevance of QT prolongation caused by the new selective serotonin antagonist ketanserin. Zehender M, Meinertz T *et al. American Journal of Cardiology* 1989; **63:** 826.

Respiration

Physiology

Panic anxiety and hyperventilation in patients with chest pain—a controlled study. Bass C, Chambers JB *et al. Quarterly Journal of Medicine* 1988; **69:** 949.

Diaphragmatic vasodilation elicited by pulmonary C-fiber stimulation. Coast JR, Romeo RM, Cassidy SS. *Respiratory Physiology* 1989; **75:** 279.

Pulmonary vascular hemodynamics in chronic lung disease patients with and without oxyhemoglobin desaturation during sleep. Fletcher EC, Luckett RA *et al. Chest* 1989; **95:** 757.

Pressure-flow behaviour of a bronchopleural fistula during mechanical ventilation with positive pressure. Fontan JJP, Ray AO. *Journal of Applied Physiology* 1989; **66:** 1789.

Peak expiratory flow in symptomless elderly smokers and ex-smokers. Gregg I, Nunn AJ. *British Medical Journal* 1989; **298:** 1071.

Effect of cardiac output on gravity-dependent and nondependent inequality in pulmonary blood flow. Hakim TS, Lisbona R, Dean GW. *Journal of Applied Physiology* 1989; **66:** 1570.

Flow-volume curves in snorting patients with and without obstructive sleep apnea. Hoffstein V, Wright S, Zamel N. *American Review of Respiratory Disease* 1989; **139:** 957.

Oxygen-mediated impairment of human pulmonary endothelial cell growth: evidence for a specific threshold of toxicity. Martin WJ II, Kachel DL. *Journal of Laboratory and Clinical Medicine* 1989; **113:** 413.

Pulmonary flow resistance. Milic-Emili J. *Lung* 1989; **167:** 141.

Effect of aging on estimates of hypercapnic ventilatory response during sleep. Naifeh KH, Severinghaus JW *et al. Journal of Applied Physiology* 1989; **66:** 1956.

New regression equations for predicting peak expiratory flow in adults. Nunn AJ, Gregg I. *British Medical Journal* 1989; **298:** 1068.

Opioid inhibition of neurally mediated mucus secretion in human bronchi. Rogers DF, Barnes P. *Lancet* 1989; **1:** 930.

Changes in pneumonectomy-space gas tensions. Simonsen L, Halkier E *et al. Scandinavian Journal of Clinical and Laboratory Investigation* 1989; **49:** 110.

Chronic obstructive pulmonary disease: risk factors, pathophysiology and pathogenesis. Snider GL. *Annual Review of Medicine* 1989; **40:** 411.

Molecular biology in respiratory disease. Stockley RA. *Clinical Science* 1989; **76:** 343.

No effect of brain blood flow on ventilatory depression during sustained hypoxia. Suzuki A, Nishimura M *et al. Journal of Applied Physiology* 1989; **66:** 1674.

Collapsibility of the human upper airway during the normal sleep. Wiegand L, Zwillich CW, White DP. *Journal of Applied Physiology* 1989; **66:** 1800.

Treatment and medication

Effect of incentive spirometry on diaphragmatic function after surgery. Chuter TAM, Weissman C *et al. Surgery* 1989; **105:** 488.

Buspirone, an anxiolytic drug that stimulates respiration. Garner SJ, Eldridge FL *et al. American Review of Respiratory Disease* 1989; **139:** 946.

Systemic gas embolism complicating mechanical ventilation in the adult respiratory distress syndrome. Marini JJ, Culver BH. *Annals of Internal Medicine* 1989; **110:** 699.

Preoperative assessment as a predictor of mortality and morbidity after lung resection. Markos J, Mullan BP *et al. American Review of Respiratory Disease* 1989; **139:** 902.

Noninvasive face mask ventilation in patients with acute respiratory failure. Meduri GU, Conoscenti CC *et al. Chest* 1989; **95:** 865.

The effects of nitrazepam and flunitrazepam on oxygen desaturation during sleep in patients with stable hypoxemic nonhypercapnic COPD. Midgren B, Hansson L *et al. Chest* 1989; **95:** 765.

Jet flow-regulated expiratory resistance to maintain constant CPAP during the entire respiratory phase. Nishimura M, Takezawa J *et al. Chest* 1989; **95:** 876.

A new pendant oxygen-conserving cannula which allows pursed lips breathing. Tiep BL, Burns M, Hererra J. *Chest* 1989; **95:** 857.

Central nervous system

Physiology

Evidence for a role of oxygen radicals in cerebral ischemic injury. Beckman JS, Liu TH *et al.* In: Ginsberg MD, Dietrich WD, eds. *Cerebrovascular disease: 16th research (Princeton) conference.* NY: Raven Press, 1989: 373.

Endogenous sleep-promoting substances and sleep regulation. Borbely AA, Tobler I. *Physiological Reviews* 1989; **69:** 605.

Differential effects of flunitrazepam on human sleep in combination with flumazenil. Gaillard JM, Blois R. *Sleep* 1989; **12:** 120.

Modulation of ischemic brain damage by noradrenaline—protection by idazoxan, an alpha-2-receptor antagonist. Gustafson I, Miyauchi Y, Wieloch T. In: Ginsberg MD, Dietrich WD, eds. *Cerebrovascular disease: 16th research (Princeton) conference.* NY: Raven Press, 1989: 365.

Pseudocholinesterase activity in human cerebrospinal fluid. Kambam JR, Horton B *et al. Anesthesia and Analgesia* 1989; **68:** 486.

Oxygen radicals in cerebral ischemia. Kontos HA. In: Ginsberg MD, Dietrich WD, eds. *Cerebrovascular disease: 16th research (Princeton) conference.* NY: Raven Press, 1989: 365.

Oxygen toxicity protecting enzymes in aging and Parkinsons disease. Marttila RJ, Rinne UK. In: Calne DB *et al.*, eds. *Parkinsonism and aging. Aging, Vol. 36.* NY: Raven Press, 1989: 89.

Comparison of neuronal loss in Parkinson's disease and aging. McGeer PL, Itagaki S *et al.* In: Calne DB *et al.*, eds. *Parkinsonism and aging. Aging, Vol. 36.* NY: Raven Press, 1989: 25.

Muscle fibre size and number following immobilisation atrophy. Nicks DK, Beneke WM *et al. Journal of Anatomy* 1989; **163:** 1.

Cerebral hyperemia, stroke, and transfusion in sickle cell disease. Prohovnik I, Pavlakis SG *et al. Neurology* 1989; **39:** 344.

Physiological sleep tendency and ability to maintain alertness at night. Sugarman JL, Walsh JK. *Sleep* 1989; **12:** 106.

The dopamine motor system. Wooten GF, Trugman JM. *Movement Disorders* 1989; **4** (Suppl. 1): S38.

Treatment and medication

Neuropsychological deficit and emotional disturbance in head-injured patients. Bornstein RA, Miller HB, Vanschoor JT. *Journal of Neurosurgery* 1989; **70:** 509.

Doppler diagnosis in cases of acute stroke. Chambers BR, Merory JR, Smidt V. *Medical Journal of Australia* 1989; **150:** 382.

Approach to management of the heartbeating 'brain dead' organ donor. Darby JM, Stein K *et al. Journal of the American Medical Association* 1989; **261:** 2222.

Effects of nimodipine on cerebral blood flow and cerebrospinal fluid pressure after cardiac arrest: correlation with neurologic outcome. Forsman M, Aarseth HP *et al. Anesthesia and Analgesia* 1989; **68:** 436.

Protective effects of the NMDA antagonist, MK-801, on focal ischemic brain damage. Graham DJ, Ozyurt E *et al.* In: Ginsberg MD, Dietrich WD, eds. *Cerebrovascular disease: 16th research (Princeton) conference.* NY: Raven Press, 1989: 65.

Treatment of muscular dystrophies. Kingston WJ, Moxley RT. *General Pharmacology* 1989; **20:** 263.

The cardio-protective features of tricyclic antidepressants. Manoach M, Varon D *et al. General Pharmacology* 1989; **20:** 269.

Overcoming pharmacokinetic problems in the treatment of Parkinson's disease. Obeso JA, Vaamonde J *et al. Movement Disorders* 1989; **4** (Suppl. 1)**:** S70.

Nimodipine and the 'no-reflow phenomenon'—experimental triumph, clinical failure? Prough D, Furberg CD. *Anesthesia and Analgesia* 1989; **68:** 431.

Effect of the NMDA antagonist MK-801 in animal models of focal and global cerebral ischemia. Shearman GT. In: Ginsberg MD, Dietrich WD, eds. *Cerebrovascular disease: 16 research (Princeton) conference.* NY: Raven Press, 1989: 73.

Clozapine: an antipsychotic agent in Parkinson's disease? Wolters E Ch., Hurwitz TA *et al. Clinical Neuropharmacology* 1989; **12:** 83.

'Brain death' and organ retrieval. Youngner SJ, Landefeld CS *et al. Journal of the American Medical Association* 1989; **261:** 2205.

Endocrine and metabolic

Physiology

Ketone body production and disposal: effects of fasting, diabetes, and exercise. Balasse EO, Fery F. *Diabetes/Metabolism Reviews* 1989; **5:** 247.

Ventilation-perfusion mismatching in acute severe asthma: effects of salbutamol and 100% oxygen. Ballester E, Reyes A. *et al. Thorax* 1989; **44:** 251.

Vasopressin: a regulator of adrenal glucocorticoid production? Brooks VL, Blakemore LJ. *American Journal of Physiology* 1989; **256** (No. 4 Part 1)**:** E566.

Increased intraoperative cardiovascular morbidity in diabetics with autonomic neuropathy. Burgos LG, Ebert TJ *et al. Anesthesiology* 1989; **70:** 591.

Raised plasma levels of atrial natriuretic peptides in Addison's disease. Cappuccio FP, Markandu ND *et al. Journal of Endocrinological Investigation* 1989; **12:** 205.

Obesity as a risk factor in drug-induced organ injury. III. Increased liver and kidney injury by furosemide in the obese overfed rat. Corcoran GB, Salazar DE *et al. Toxicology and Applied Pharmacology* 1989; **98:** 12.

Recent insight into the structure and function of the glucocorticoid receptor. Distelhorst CW. *Journal of Laboratory and Clinical Medicine* 1989; **113:** 404.

Lipoprotein lipase: a multifunctional enzyme relevant to common metabolic diseases. Eckel RH. *New England Journal of Medicine* 1989; **320:** 1060.

Natriuretic factors and lithium clearance in patients with the syndrome of in appropriate antidiuretic hormone. Gross P, Lang R *et al. European Journal of Clinical Investigation* 1989; **19:** 11.

Update on somatomedin. Hall K, Brismar K, Thoren M. *Acta Paediatrica Scandinavica* 1988; Suppl. **347:** 87.

Effects of prostaglandin E2 and D2 on the release of vasopressin and oxytocin. Hashimoto H, Noto T, Nakajima T. *Prostaglandins, Leukotrienes and Essential Fatty Acids* 1989; **36:** 9.

The adrenocortical system responds slowly to removal of corticosterone in the absence of concurrent stress. Jacobson L, Akana SF *et al. Endocrinology* 1989; **124:** 2144.

Thyroid hormone metabolism in hypermetabolic patients with haematological disorders. Kirkegaard C, Hasselbalch H *et al. Hormone and Metabolic Research* 1989; **21:** 145.

The intracellular itinerary of insulin and insulin receptors. Marshall S. In: Draznin B *et al.*, eds. *Molecular and cellular biology of diabetes mellitus, Vol. 2 insulin action.* NY: Alan R. Liss, 1989: 35.

The effects of intracerebroventricularly injected corticotropin-releasing factor (CRF) on the central nervous system: behavioural and biochemical studies. Matsuzaki I, Takamatsu Y, Moroji T. *Neuropeptides* 1989; **13:** 147.

The relationship between the ventilation and lactate thresholds folowing normal, low and high carbohydrate diets. McLellan TM, Gass GC. *European Journal of Applied Physiology and Occupational Physiology* 1989; **58:** 568.

Monocyte activation after burns and endotoxemia. Moore FD Jr, Davis CF. *Journal of Surgical Research* 1989; **46:** 350.

Osmotic thresholds for AVP release with the use of plasma and urine AVP and free water clearance. Moses AM. *American Journal of Physiology* 1989; **256** (No. 4 Part 2)**:** R892.

Ventilatory and heart rate responses to hypoxia and hypercapnia in patients with diabetes mellitus. Nishimura M, Miyamoto K *et al. Thorax* 1989; **44:** 257.

Ketone body metabolism: a physiological and clinical overview. Nosadini R, Avogaro A *et al. Diabetes/Metabolism Reviews* 1989; **5:** 299.

Muscle dysfunction in malnourished patients. Pichard C, Jeejeebhoy KN. *Quarterly Journal of Medicine* 1988; **69:** 1021.

Abnormal diurnal rhythm of plasma vasopressin and urinary output in patients with enuresis. Rittig S, Knudsen UB *et al. American Journal of Physiology* 1989; **256** (No. 4 Part 2)**:** F664.

Postoperative hypophosphatemia: A multifactorial problem. Robinson MF. *Nutrition Reviews* 1989; **47:** 111.

Physiology of magnesium metabolism and the important role of magnesium in potassium deficiency. Rude RK. *American Journal of Cardiology* 1989; **63:** G31.

Cerebral blood flow and the thermal properties of the brain—a preliminary analysis. Salcman M, Moriyama E *et al. Journal of Neurosurgery* 1989; **70:** 592.

Islet blood flow following insulin administration. Sparrow RA, Beckingham IJ. *Journal of Anatomy* 1989; **163:** 75.

Promotion and subsequent inhibition of plasminogen activation after administration of intravenous endotoxin to normal subjects. Suffredini AF, Harpel PC, Parrillo JE. *New England Journal of Medicine* 1989; **320:** 1165.

The interaction of arginine vasopressin and oxytocin with bovine adrenal medulla cells. Taylor AH, Whitley G St J, Nussey SS. *Journal of Endocrinology* 1989; **121:** 133.

Molecular mechanisms of insulin resistance. Taylor SI. In: Draznin B *et al.* eds. *Molecular and cellular biology of diabetes mellitus, Vol. 2 insulin action.* NY: Alan R. Liss, 1989: 97.

Treatment and medication

Dose dependency of furosemide-induced sodium excretion. Andreasen F, Lauridsen IN *et al. Journal of Pharmacology and Experimental Therapeutics* 1989; **248:** 1182.

Effects of the GABAergic agent sodium valproate on the arginine vasopressin responses to hypertonic stimulation and upright posture in man. Chiodera P, Gnudi A *et al. Clinical Endocrinology* 1989; **30:** 389.

Systemic delivery of insulin through eyes to lower the glucose concentration. Chiou GCY, Chuand CY, Chang MS. *Journal of Ocular Pharmacology* 1989; **5:** 81.

Acid-base disorders in critical care medicine. Fencl V, Rossing TH. *Annual Review of Medicine* 1989; **40:** 17.

Effect of transdermal clonidine on the endocrine responses to insulin-induced hypoglycemia in essential hypertension. Guthrie G P Jr, Kotchen TA, Van Loon G. *Clinical Pharmacology and Therapeutics* 1989; **45:** 417.

Bedside monitoring of the blood glucose level: the high cost of reliable results. Innanen VT, Korogyi N *et al. Canadian Medical Association Journal* 1989; **140:** 899.

Furosemide and dopamine in malarial acute renal failure. Lumlertgul D, Keoplung D *et al. Nephron* 1989; **52:** 40.

A comparison of the effects of ibuprofen and indomethacin upon renal haemodynamics and electrolyte excretion in the presence and absence of frusemide. PASSMORE AP, COPELAND S, JOHNSTON GD. *British Journal of Clinical Pharmacology* 1989; **27:** 483.

Sensitivity to insulin during treatment with atenolol and metoprolol: a study of effects on carbohydrate and lipoprotein metabolism in hypertensive patients. POLLARE T, LITHELL H *et al. British Medical Journal* 1989; **298:** 1152.

The combined use of insulin and sulfonylurea therapy in patients with non-insulin dependent diabetes mellitus. REAVEN GM, FRAZE E *et al. Hormone and Metabolic Research* 1989; **21:** 132.

Insulin secretion and glucose tolerance in non-insulin dependent diabetic patients after chronic nifedipine treatment. TENTORIO A, GHILARDI G *et al. European Journal of Clinical Pharmacology* 1989; **36:** 311.

Pain

Physiology

The involvement of opioid peptides in stress-induced analgesia in the slug Arion ater. DALTON LM, WIDDOWSON PS. *Peptides* 1989; **10:** 9.

Anatomy, physiology and pharmacolaogy of the periaqueductal gray contribution to antinociceptive controls. REICHLING DB, KWIAT GC, BASBAUM AI. In: FIELDS HL, BESSON JM, eds. *Pain modulation.* Amsterdam: Elsevier, 1988: 31.

Anatomy and physiology of descending control of nociceptive responses of dorsal horn neurons—comprehensive reviews. WILLIS WD. In: FIELDS HL, BESSON JM, eds. *Pain modulation.* Amsterdam: Elsevier, 1988: 1.

Treatment and medication

Studies of PAG/PVG stimulation for pain relief in humans. BARBARO NM. In: FIELDS HL, BESSON JM, eds. *Pain modulation.* Amsterdam: Elsevier, 1988: 165.

Comparison of analgesic requirements after liver transplantation and cholecystectomy. EISENACH JC, PLEVAK DJ *et al. Mayo Clinic Proceedings* 1989; **64:** 356.

Effects of morphine given in the brain stem on the activity of dorsal horn nociceptive neurons. FEBHART GF, JONES SL. In: FIELDS HL, BESSON JM, eds. *Pain modulation.* Amsterdam: Elsevier, 1988: 229.

Intrathecal administration—methodological considerations. HAMMOND DL. In: FIELDS HL, BESSON JM, eds. *Pain modulation.* Amsterdam: Elsevier, 1988: 313.

Intrapleural analgesia for post-thoracotomy pain and blood levels of bupivacaine following intrapleural injection. KAMBAM JR, HAMMON J *et al. Canadian Journal of Anaesthesia* 1989; **36:** 106.

Spinal cord stimulation in management of chronic pain—a 9-year experience. MEGLIA M, CIONI B, ROSSI GF. *Journal of Neurosurgery* 1989; **70:** 519.

Sites of action of opiates in production of analgesia. YAKSH TL, ALRODHAN NRF, JENSEN TS. In: FIELDS HL, BESSON JM, eds. *Pain modulation.* Amsterdam: Elsevier, 1988: 371.

Other

Physiology

Molecular mechanisms of osmosis. KIIL F. *American Journal of Physiology* 1989; **256** (No. 4 Part 2)**:** R801.

Treatment and medication

The use of ranitidine in prophylaxis for stress ulceration. GAUTHIER A, PASCAL JP. In: MIGNON M, GALMICHE J, eds. *Safe and Effective control of acid secretion.* Montrouge: John Libbey, 1988: 293.

Change in hepatic function, hemodynamics, and morphology after liver transplant: physiological effect of therapy. MILLIKAN WJ, HENDERSON M *et al. Annals of Surgery* 1989; **209:** 513.

Mechanisms of nonsteroidal anti-inflammatory drug-induced gastric damage. SCHOEN RT, VENDER RJ. *American Journal of Medicine* 1989; **86:** 449.